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SPORADIC INFECTIONS CAUSED BY *SALMONELLA SUIPESTIFER* AND *SALMONELLA ORANIENBURG**

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SPORADIC cases of *Salmonella suipestifer* infection continue to arouse interest because of their variable clinical manifestations. In the period of one year, 6 patients with this infection were observed at the Boston City Hospital. Two additional patients whom we originally believed to be infected with the organism were subsequently found to be infected with *S. oranienburg*, a closely related bacterium. This report presents the clinical, laboratory and bacteriologic findings of the 8 cases mentioned and a brief discussion in which the bacteriologic identification is emphasized.

CASE REPORTS

CASE 1. A. C., a 63-year-old man, was readmitted on November 30, 1940, after having been discharged 6 months previously with a diagnosis of acute posterior coronary thrombosis, chronic bronchitis and arteriosclerotic heart disease with mild cardiac decompensation. Subsequently he was essentially well until 9 days before the present admission, when there was an onset of shaking chills followed by drenching sweats that recurred every evening. In addition there were marked irritability, intermittent mental confusion, anorexia, urinary frequency and progressive weakness.

Physical examination showed a chronically ill-appearing male who was moderately confused. The chest was emphysematous. Moist rales were present at the base of each lung posteriorly. The heart appeared to be normal. The blood pressure was 110/60. The liver edge was felt 3 cm. below the costal margin. The spleen was not palpable. The left leg was shortened, and the left femur was thickened along its entire shaft. The temperature was 102°F., the pulse 90, and the respirations 28. The hemoglobin was 90 per cent (Sahli). The red-cell count was 4,480,000 and the white-cell count 13,900, with 78 per cent polymorphonuclear leukocytes, 16 per cent lymphocytes and 6 per cent monocytes. The urine contained a heavy trace of albumin and many leukocytes. The blood Hinton reaction was negative. The plasma nonprotein nitrogen was 48 mg. per 100 cc.

The patient's course was one of gradual decline with periods of temporary improvement. Anorexia, nausea, weakness, delirium, chills and fever were the salient features. At no time was there any diarrhea or evidence of cardiac failure. During the first 10 days of hospitalization the temperature was persistently elevated, varying between 99.5 and 102°F. Thereafter there was a remittent type of fever with febrile episodes lasting for 2 to 5 days, with intervening periods of subnormal temperature of 5 to 9 days' duration. Occasionally rapid temperature rises were accompanied by shaking chills. The pulse varied between 70 and 110, and the respirations between 20 and 25. The hemoglobin fell gradually to 60 per cent. The white-cell count varied between 7500 and 15,000. Subsequent plasma nonprotein nitrogen determinations showed no significant change from the initial level of 48 mg. per 100 cc. until the last week, when there was a rise to 198 mg. The urine, which had a maximum specific gravity of 1.030, consistently contained large amounts of albumin and variable numbers of leukocytes. The results of two lumbar punctures were negative. Two electrocardiograms showed no significant abnormality.

Roentgenograms of the chest were interpreted as emphysema, except for a film 2 days before death that showed a patchy infiltration at the base of the right lung. A film of the left femur showed changes consistent with osteitis fibrosa cystica within the shaft.

The patient received digitalis and, toward the latter part of the illness, parenteral fluids and small transfusions. From December 25 to January 2, 1941, he received a total of 46 gm. of sulfadiazine without appreciable response, and from January 19 to 22 10 more. He became progressively weaker and died on January 29, approximately 10 weeks after the onset of the present illness. Terminally the clinical picture was that of uremia.

A blood culture taken on the day of admission was positive for *S. suipestifer*. Cultures taken on December 1, January 11, 15, 19, 24 and 29 were also positive for this organism, whereas those taken on January 6 and 16 were sterile. Neither of the sterile cultures was taken at a time when the patient was receiving chemotherapy. Between December 1 and January 29 seven urine cultures were positive for *S. suipestifer* and one taken on January 6 was sterile. Two stool cultures, a culture of sputum and a culture of prostatic secretion failed to yield this organism. On four occasions between December 8 and January 20 the patient's serum agglutinated his own organism and stock strains of *S. suipestifer* to a dilution of 1:640.

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Autopsy (performed 2 hours after death). The heart was moderately enlarged and weighed 610 gm. There was a slight dilatation of the apex of the heart, with softening of the muscle in this region and thickening of the overlying pericardium. On section the myocardium of the apex of the left ventricle was markedly thinned and on the underlying endocardial surface there was a large, firmly adherent, yellow thrombus which almost filled the lower half of the left ventricular chamber. The coronary arteries showed moderate sclerotic changes. The heart valves were normal. The right lower lobe of the lung showed a patchy pneumonic consolidation with multiple miliary abscesses. Elsewhere the lungs appeared normal. The spleen was slightly enlarged and at one pole there was a small yellow infarct. The liver was normal. The gastrointestinal tract was normal, except for a small duodenocolic fistula. The kidneys showed no significant abnormality other than a small infarct in the right kidney. The mucosal surface of the bladder was gray-black and roughened about the trigone. The left femur showed a fusiform dilatation of the shaft with destruction and replacement of bone by firm, gray tissue.

Histologically, the myocardium of the apex of the heart showed almost complete replacement by dense scar tissue. The attached mural thrombus showed evidence of organization in the deeper portion and superficially it was composed of fibrin, platelets and leukocytes. These changes indicated that the myocardial lesion was of at least several months' duration. The splenic infarct appeared recent in origin. The liver parenchyma was normal. The kidneys showed minimal changes that were consistent with slight benign nephrosclerosis. Sections of the left femur were consistent with localized osteitis fibrosa cystica.

A post-mortem culture of the heart's blood was sterile. A swab inserted in the endocardial thrombus was positive for *S. suipestifer*. Type 29 pneumococcus was the only organism cultured from the right lower lobe of the lung. Cultures of the spleen, of the liver, of bile aspirated from the hepatic duct and of the feces were negative for *S. suipestifer*. Gram–Weigert and MacCallum–Goodpasture stains of sections of myocardium, of the endocardial thrombus and of the splenic infarct showed no bacteria, so that it was impossible to prove satisfactorily that the endocardial thrombus was the focus responsible for the prolonged septicemia, in spite of the fact that the endocardial thrombus yielded *S. suipestifer*, while the heart's blood was sterile.

The pathological diagnoses were as follows: myocardial infarction, old, with mural thrombus; bronchopneumonia, with miliary abscesses, right lower lobe; slight benign nephrosclerosis; acute cystitis; small duodenocolic fistula; localized osteitis fibrosa cystica, left femur; surgical absence of gall bladder; and infarcts of spleen and right kidney.

Case 2. C. M., a 48-year-old man, was admitted on March 19, 1941, because of dysuria and frequency of 2 months' duration.

The temperature was 98.6°F., the pulse 110, and the respirations 20. The heart and lungs were normal. The blood pressure was 160/100. Both kidneys were palpable, and there was moderate costovertebral tenderness on the right. The urine contained a heavy trace of albumin and many leukocytes. The hemoglobin was 90 per cent (Sahli), the red-cell count was 4,160,000, and the white-cell count was 12,200. The blood Hinton reaction was negative. The plasma nonprotein nitrogen level was 38 mg. per 100 cc. A retrograde pyelogram showed a single large stone in the dilated pelvis of the right kidney.

The day after admission the right kidney was removed. For the first 12 postoperative days, the patient was acutely ill, with the temperature varying between 100 and 103°F.; thereafter the temperature was normal. On the 5th postoperative day, cough and pulmonary rales appeared. A roentgenogram was interpreted as indicating bronchopneumonia. At this time the patient was given 6 gm. of sulfathiazole daily for 1 week. He developed an anemia, with the hemoglobin falling to 60 per cent (Sahli), and the red-cell count to 3,000,000. Throughout the illness the white-cell count remained moderately elevated, varying between 10,000 and 20,000. Differential counts taken from the 2nd to 5th week of hospitalization showed from 60 to 80 per cent polymorphonuclear leukocytes and from 8, to 20 per cent monocytes, the rest of the cells being lymphocytes. The albumin disappeared from the urine within several days after operation; however, leukocytes were persistently present. At the time of operation, and on three subsequent occasions during the first 2 postoperative weeks, *S. suipestifer* was cultured from the wound. No preoperative urine cultures were obtained. Three blood cultures during the febrile postoperative period were sterile. Cultures of the throat, stools, urine and bile were negative for *S. suipestifer*. On the 7th postoperative day, the patient's serum agglutinated his own organism and stock strains of *S. suipestifer* to a dilution of 1:640. He was discharged well on April 26.

The resected right kidney measured 18 by 9 by 5 cm. The renal cortex was narrowed, and there was a tremendous dilatation of the calyxes and renal pelvis. A single stone, 3 cm. in diameter, was in the renal pelvis. Histologically the kidney showed changes consistent with hydronephrosis, pyelitis and slight chronic pyelonephritis. There were no abscesses in the renal parenchyma.

Case 3. I. M., a 21-year-old, unmarried woman, was admitted on February 23, 1941, because of severe, crampy right lower abdominal pain of 4 days' duration. This was accompanied by headache, feverishness, obstipation, nausea, anorexia and drowsiness. There were no chills, vomiting or diarrhea. There was no history of intercourse.

On examination the patient appeared moderately ill. The temperature was 101°F., and the pulse 120. The heart and lungs were normal. The liver and spleen could not be palpated. There was rebound tenderness in the right lower quadrant of the abdomen. The following day an exploratory laparotomy was performed. The appendix and the left fallopian tube were normal, whereas the right fallopian tube appeared markedly enlarged, thickened and reddened. There was a small amount of fibrinous exudate in the pelvis. A right salpingectomy and an appendectomy were performed. A culture of the pelvic exudate yielded *S. suipestifer*. Postoperatively the patient received 6 gm. of sulfanilamide daily for 3 days. The temperature and pulse fell slowly to normal by the 5th postoperative day. Convalescence was uneventful.

At the time of admission, the hemoglobin was 70 per cent (Sahli), the red-cell count 4,040,000, and the white-cell count 11,600. Subsequent white-cell counts varied between 7000 and 9000 with 60 to 70 per cent polymorphonuclear leukocytes and 4 to 8 monocytes, the rest of the cells being lymphocytes. The stools and urine were normal.

S. suipestifer was recovered from the pelvic exudate at operation on February 24. The same organism was recovered from cultures of the abdominal wound on three occasions during the next 3 weeks. Cultures of the throat, urine, stools, bile and cervix did not yield this

organism. On March 2, the patient's serum failed to agglutinate her own organism or stock strains of *S. suipestifer*. On five subsequent occasions between March 12 and 27, her serum agglutinated her own organism and stock strains of *S. suipestifer* to a dilution of 1:640.

The resected fallopian tube was distended with thin sanguinopurulent material. Histologically the changes were those of chronic salpingitis and pyosalpinx with a superimposed acute inflammatory reaction.

CASE 4. E. P., a 4-year-old girl, was readmitted on January 8, 1941. Three weeks previously she had been discharged from this hospital, having made an uneventful convalescence from pertussis. Except for a slight cough she was well until 1 week before the present admission, when there was an onset of fever and cough productive of blood-tinged sputum.

At the time of admission the patient appeared acutely ill. The tonsils were moderately enlarged and injected. The heart appeared to be normal. Fine rales were heard throughout the entire chest, although there was no evidence of consolidation. The remainder of the examination was negative. The temperature was 105°F., the pulse 148, and the respirations 48. Laboratory studies showed the urine to be normal. The hemoglobin was 92 per cent (Sahli), the red-cell count 5,650,000, and the white-cell count 8600, with 42 per cent polymorphonuclear leukocytes, 48 per cent lymphocytes and 10 per cent monocytes. An x-ray film of the chest was interpreted as showing bronchopneumonia in the right hilar area. The patient was given sulfathiazole, 0.5 gm. every 4 hours for 48 hours. On the 3rd hospital day, the temperature, pulse and respirations returned to normal. Convalescence was uneventful. On the 8th day, the hemoglobin was 67 per cent (Sahli) and the white-cell count 12,400, with 62 per cent polymorphonuclear leukocytes and 38 per cent lymphocytes.

A blood culture on January 9, the day after admission, was positive for *S. suipestifer*. On January 14 and 20 the patient's serum failed to agglutinate her own organism and stock strains of *S. suipestifer*. From a throat culture taken on January 15 at a time when the patient was afebrile, a Type 18-*A* pneumococcus was recovered. A urine culture on January 15 was sterile. The patient was discharged on January 26 with a diagnosis of *S. suipestifer* bacteremia and bronchopneumonia.

CASE 5. R. M., a 35-year-old man with a long history of alcoholism, was admitted on August 19, 1940. For 6 months he had had a chronic productive cough accompanied by anorexia, night sweats and loss of weight. The day of admission he developed diarrhea and frequent shaking chills.

On physical examination the patient appeared both acutely and chronically ill. The temperature was 103°F., the pulse 90, and the respirations 20. The only abnormal finding in the chest was bronchial breathing at the right lung base posteriorly. The liver was enlarged, extending 9 cm. below the right costal margin. The spleen was not palpable. The patient had a severe macrocytic anemia. There was no achlorhydria. The white-cell count was 3400, with 62 per cent polymorphonuclear leukocytes, 32 per cent lymphocytes and 6 per cent monocytes. Subsequent counts varied between 6000 and 12,000. The urines and stools were normal. Roentgenograms of the chest showed changes consistent with bronchiectasis of the right lower lobe.

The patient remained in the hospital for 8 weeks. The diarrhea subsided within 24 hours. The temperature rose to 102°F. on the 2nd day, returned to normal on the 3rd day, and for the next 10 days showed frequent rises to 99 or 100°F. Thereafter the patient was afebrile. The pulse varied between 80 and 110. The patient slowly gained weight and strength. The macrocytic anemia responded to liver therapy. The liver decreased in size. Liver-function tests on several occasions showed no impairment.

A blood culture taken on the day of admission was positive for *S. suipestifer*. Subsequent cultures of the blood, urine, stools, sputum and bile were negative for this organism. The patient's serum on August 27 and September 11 failed to agglutinate his own organism and stock strains of *S. suipestifer*. He was discharged on September 13 with a diagnosis of *S. suipestifer* septicemia, chronic alcoholism, early cirrhosis of the liver, macrocytic anemia of undetermined etiology, malnutrition and bronchiectasis.

CASE 6. W. C., a 44-year-old man, was admitted on October 23, 1940. There was a history of chronic alcoholism. For the past 4 months there had been an intermittent productive cough. Two weeks before admission, the patient had several shaking chills which were followed by sweats. Two days later, he experienced a pleuritic type of pain in the region of the right lower chest and his cough became productive of brownish sputum. The present illness was attended by malaise and dull epigastric pain.

Physical examination revealed a well-developed, poorly nourished man who appeared moderately ill. The tongue, which showed moderate atrophy of the papillae, exhibited a coarse tremor. There was slightly diminished resonance over the left chest anteriorly and posteriorly and occasional rales were heard in these areas. The heart appeared to be normal. The blood pressure was 154/90. The liver edge was felt at the right costal margin. The spleen was not palpable. Physical examination was otherwise negative.

The temperature was 100.8°F., the pulse 112, and the respirations 28. The hemoglobin was 89 per cent (Sahli). The red-cell count was 3,850,000. The white-cell count was 4600, with 54 per cent polymorphonuclear leukocytes, 44 per cent lymphocytes and 2 per cent monocytes. Subsequent counts varied between 4800 and 5200. Repeated examinations of the urine and stools were normal. The blood Hinton reaction was negative. On repeated examinations of the sputum, no tubercle bacilli were present. A roentgenogram showed the lung fields to be clear.

The patient received supportive treatment supplemented by vitamin therapy. The temperature remained elevated for the 1st week of hospitalization, varying between 99 and 101°F., and thereafter was normal. The pulse varied between 70 and 90. On the 4th hospital day, the patient became jaundiced, with an icteric index of 25. Four days later the jaundice had subsided. At the onset of the jaundice the liver edge was palpable 4 cm. below the costal margin. Recovery was gradual.

A blood culture on October 29, 6 days after admission, yielded *S. suipestifer*. Subsequent blood cultures taken on October 31 and November 1 and 2 were sterile. On October 28, a Type 14 pneumococcus was recovered from the sputum. A culture of urine on November 2 and stool cultures on November 2 and 4 were negative for *S. suipestifer*. The patient's serum on November 2, 8 and 19 agglutinated his own organism and stock strains of *S. suipestifer* to a dilution of 1:640.

The patient was discharged on November 24 with a diagnosis of chronic alcoholism, acute infectious hepatitis, early cirrhosis of the liver, deficiency of vitamin B complex and *S. suipestifer* bacteremia.

Certain findings in this small series of 6 cases of *S. suipestifer* infection deserve comment. Only 1 case occurred in a child, the remaining 5 in adults. In no case was the source of infection determined.

Harvey[1] divided 71 cases of sporadic *S. suipestifer* infection into clinical groups. Most numerous were the typhoidlike infections, in which there were no localizing signs. Fever, anorexia, vomiting, headache and diarrhea were the commonest symptoms. The pulse was usually rapid. Mild bronchitis was frequent in older patients. A second large group of patients had pulmonary involvement, as evidenced by bronchopneumonia, occasional lobar pneumonia, pleurisy with effusion and empyema. A third group included suppurative bone and joint lesions due to this organism. A fourth group was comprised of infections complicating surgical procedures. In additional groups were placed the more unusual complications, such as involvement of the nervous system, endocarditis and urinary-tract infection.

Two of our 6 cases of *S. suipestifer* infection fall into the group with typhoidlike symptoms. In Case 1, however, the anatomical findings suggested that an endocardial thrombus might have been a focus of infection, although this could not be established with certainty. In this respect, the case was more analogous to a *S. suipestifer* endocarditis, which has occasionally been observed.[2–5]

In 5 cases there was clinical or roentgenologic evidence of pulmonary involvement. In 2 cases (Cases 4 and 6) the pulmonary complications were a prominent feature in the present illness, while in 2 others (Cases 1 and 2) they appeared to be incidental. In Case 5, the pre-existing bronchiectasis seemed unrelated to the present illness. In all 6 cases, cultures of the sputum or throat failed to yield *S. suipestifer*. In Cases 4 and 6, pneumococci recovered from the sputum and from a throat culture may have been responsible for the pulmonary infection. In Case 1, at autopsy there was a bronchopneumonia. Cultures from the affected lobe yielded only Type 29 pneumococcus. In only 6 of the 24 cases of *S. suipestifer* infection with pulmonary complications described by Harvey[1] was there bacteriologic proof that this organism was responsible for the pulmonary changes. Kuttner and Zepp[6] describe the case of a two-year-old child who had *S. suipestifer* bacteremia. At autopsy this organism was recovered from the heart's blood, whereas a Type 3 pneumococcus and the influenza bacillus were the only organisms present in cultures of the lungs. These observations suggest that pulmonary involvement occurring during the course of this infection may be caused by other bacteria that may be regarded as accompanying or secondary infections.

Cases of *S. suipestifer* infection in which the urinary-tract infection has a prominent role in the clinical symptoms are unusual.[1] In Case 2, a large single renal calculus causing obstruction was associated with *S. suipestifer* infection in the involved kidney.

Acute abdominal conditions resulting from *S. suipestifer* infection have been relatively frequent. Kuttner and Zepp[7] described a case of fibrinous peritonitis due to this organism. Walker, Weiss and Nye[8] described a case of *S. suipestifer* bacteremia complicated by a large splenic abscess. From a case with chronic cholecystitis, they cultured from the gall bladder an organism which although not fully identified was presumed to be *S. suipestifer*. In Case 3 of our series, there was a unilateral salpingitis with a localized fibrinous peritonitis from which *S. suipestifer* was cultured. Herring and Nicholson[9] described a case with bilateral acute salpingitis and pelvic peritonitis due to this organism. TenBroeck and his co-workers[10] described a *S. suipestifer* infection in association with an induced abortion and subsequent sepsis. Boller[11] observed a *S. suipestifer* infection associated with postpartum sepsis. In a case described by Gray,[12] *S. suipestifer* septicemia was associated with multiple infected uterine myomas.

Certain other clinical findings were of interest in our series. Fever was present in 5 cases at the time of admission and developed in the other postoperatively. Two patients had chills. Diarrhea occurred only once. Relative bradycardia occurred once. There was enlargement of the liver in 3 cases; in 2, however, there was a history of chronic alcoholism. Jaundice occurred in 1 case and was of brief duration. Splenomegaly was not observed. Chemotherapy, which was employed in 4 cases, did not seem to have a beneficial effect in any. Four patients were debilitated prior to the onset of the illness, either by previous illness or chronic alcoholism.

The blood findings deserve mention. A moderate anemia was present or developed during the course of the illness in 4 cases; in several of them, however, chemotherapy may have been a factor in its production. In 3 cases the initial white-cell count was low or normal, whereas in 3 it was elevated. In 2 cases the urine contained albumin and leukocytes.

In 4 of the 5 cases in which blood cultures were made, the organism was recovered. Urine cultures were positive in only 1 case. Stool cultures were

negative in every case. Prostatic secretion in 1 case and culture of the cervix in 1 did not yield this organism. Sputum or throat cultures were made in every case, but *S. suipestifer* was not recovered. Cultures of the bile were made in 3 cases and gave negative results. Cultures of the wounds in the 2 cases with surgical complications gave repeatedly positive results. In 4 cases, the patients' serums agglutinated their organisms. In 3, this was manifest during the third or fourth week of illness and may have appeared earlier. In 1 case, the duration of the illness could not be ascertained. In 2 cases, the patients' serums did not agglutinate their organisms by the fourth week and no subsequent studies were made.

TABLE 1. *Fermentation Reactions.*

ORGANISM	SUGAR FERMENTATIONS*										H_2S PRODUCTION
	DEXTROSE	LACTOSE	SUCROSE	XYLOSE	ARABINOSE	RHAMNOSE	INOSITE	MANNITE	DULCITE	TREHALOSE	
S. cholerae-suis var. *kunzendorf*	AG	–	–	AG	–	AG	–	AG	–†	–	+
S. cholerae-suis	AG	–	–	AG	–	AG	–	AG	–	–	–
S. paratyphi C	AG	–	–	AG	AG	AG	–	AG	AG	AG	+
S. oranienburg	AG	–	–	AG	AG	AG	–	AG	AG	AG	+
Case 1	AG	–	–	AG	–	AG	–	AG	–†	–	+
Case 2	AG	–	–	AG	–	AG	–	AG	–	–	+
Case 3	AG	–	–	AG	–	AG	–	AG	–†	–	+
Case 4	AG	–	–	AG	–	AG	–	AG	–	–	+
Case 5	AG	–	–	AG	–	AG	–	AG	–†	–	+
Case 6	AG	–	–	AG	–	AG	–	AG	–	–	+
Case 7	AG	–	–	AG	AG	AG	–	AG	AG	AG	+
Case 8	AG	–	–	AG	AG	AG	–	AG	AG	AG	+

*"AG" = fermentation with the formation of acid and gas; "–" = no fermentation.
†Delayed fermentation (5 to 14 days).

S. suipestifer is a gram-negative motile bacillus that can be separated from other members of the Salmonella group by its selective fermentation reactions and by agglutinations with specific antiserums. It belongs in Group C of the Kauffmann–White classification[13] of the typhoid-paratyphoid organisms. The organisms in Group C have in common at least one of the two somatic antigens V and VII. The term *"Salmonella suipestifer"* includes several organisms that have both the somatic antigens VI and VII but differ slightly in their flagellar antigenic components and in their selective fermentation reactions (Table 1). *S. cholerae-suis*, var. *kunzendorf* (monophasic, western European type of *S. suipestifer;* Group II of Andrewes[14]) is a monophasic organism with group flagellar antigens 1, 3, 4 and 5, which are shared by certain other members of the Salmonella group. *S. cholerae-suis* (diphasic, American strain of *S. suipestifer*; Group I of Andrewes) exists in two phases. In one phase, this organism has the group flagellar antigens 1, 3, 4 and 5, which are identical with those of the monophasic organism (*S. cholerae-suis*, var. *kunzendorf*), whereas in the other phase this organism has only the type-specific flagellar antigen *c*. *S. paratyphi C* (*Bacterium paratyphosum C.*; eastern European type of *S. suipestifer*; Hirschfeld type) is likewise diphasic and may occur in the group phase with flagellar components 1, 4 and 5 or in the type-specific phase with the flagellar antigen *c*. In addition, there are several allied types of *S. suipestifer* that differ slightly in their selective fermentation reaction but have the same antigenic structure.

According to Kauffmann,[13] the majority of diphasic Salmonella organisms tend to occur predominantly in the specific phase when freshly isolated. Such an organism gives rise to substrains that occur in the specific phase and the group phase.[13, 14] It is apparent that organisms of the diphasic strain can occur predominantly in the nonspecific phase in a given culture. In this event, *S. cholerae-suis*, a diphasic organism, would be antigenically indistinct from *S. cholerae-suis*, var. *kunzendorf*, a monophasic type. It was formerly assumed that monophasic types never gave rise to substrains of the diphasic type. This view has been refuted by Bruner and Edwards,[15, 16] who were able to obtain diphasic strains from monophasic strains by special culture technic. Under ordinary cultural conditions, however, this change did not occur.

The six strains of *S. suipestifer* isolated from our cases belong to the type *S. cholerae-suis*, var. *kunzendorf*, a monophasic organism. In America, infections in man from both the diphasic type (*S. cholerae-suis*) and the monophasic type (*S. cholerae-suis*, var. *kunzendorf*) have been observed. In recent years, however, the monophasic type has been found more frequently.[4, 6, 7, 16] To our knowledge, the Hirschfeld strain (*S. paratyphi C*) has not been found in this country.

From selective fermentation reactions, our six strains belonged to the monophasic type. For absolute identification, agglutinin absorption studies

were employed. Serums were prepared by immunizing rabbits with formalized saline suspensions of the three types of *S. suipestifer*. Serum prepared from *S. cholerae-suis* (diphasic type) was repeatedly absorbed with heavy suspensions of *S. cholerae-suis*, var. *kunzendorf* (monophasic type), until the absorbed serum failed to agglutinate suspensions of monophasic organisms but agglutinated suspensions of the diphasic organisms (*S. -holerae-suis* and *S. paratyphi C*) to a dilution of 1:320. The absorbed serum failed to agglutinate the organisms recovered from 5 of our 6 cases. In the sixth case the organism was lost before complete serologic identification was established.

The suspensions of *S. suipestifer* from the 5 cases tested with the absorbed serum were prepared as follows. Mice were injected intraperitoneally with each of the five strains. The organisms were recovered from cultures of the heart's blood of the autopsied mice. Isolated colonies were transferred to agar slants, and after incubation for eighteen hours, saline suspensions were made from the slants. Complete fermentation reactions and agglutination tests with stock *S. suipestifer* serum were made on the organisms in the saline suspensions in order to assure their identity with the organism injected into the mouse. A drop of 40 per cent formaldehyde was then added to the eighteen-hour saline suspensions, which were subsequently tested with the diphasic strain of *S. suipestifer* serum absorbed with the monophasic strain. Owing to the use of multiple colonies of each strain for testing with the absorbed serum, the possibility that the diphasic organisms occurred only in the group phase rather than in the specific phase was extremely unlikely. This procedure, together with the selective fermentation reactions, identified our five organisms as *S. cholerae-suis*, var. *kunzendorf*.

Stock strains of the three types of *S. suipestifer* and also the organisms recovered from our cases were injected intraperitoneally and subcutaneously into mice. The animals injected intraperitoneally died within eighteen hours, whereas those injected subcutaneously died within two to nine days. In every case the organisms were recovered from the heart's blood and spleen.

Rabbits in which the serums were found to contain no antibodies to *S. suipestifer* and related organisms were injected subcutaneously with the three different types of *S. suipestifer*. Those injected with *S. cholerae-suis* and *S. cholerae-suis*, var. *kunzendorf*, died within five to nine days. At autopsy no gross anatomic changes were observed, but histologically focal areas of necrosis were present in the liver. The organism was recovered from the heart's blood, liver and spleen in every case. The rabbit injected with *S. paratyphi C* (Hirschfeld type) did not become ill and did not develop antibodies. According to TenBroeck,[10] this type when injected subcutaneously does not kill rabbits. One rabbit in which the serum was found to contain no agglutinins to *S. suipestifer* and allied organisms was given a heavy suspension of *S. cholerae suis* by stomach tube and did not become ill or develop agglutinins to this organism.

In addition to the six strains of *S. suipestifer*, we isolated two other organisms that we originally believed to be *S. paratyphi C*; they were subsequently identified for us by Dr. Siegbert Bornstein[17] as *S. oranienburg*, a closely related organism. The case reports and bacteriologic studies of the 2 cases of *S. oranienburg* infection are reported below.

Case Reports

Case 7. A. W., a 13-year-old boy, was admitted on October 15, 1941, complaining of fever, aching of the knees, anorexia and headache of 1 week's duration. There was no vomiting or diarrhea.

Physical examination revealed enlarged cervical and axillary nodes. The lungs were normal. An apical systolic murmur was present in the heart, which was not enlarged. The tip of the spleen was palpable beneath the left costal margin. The liver was not enlarged. The remainder of the examination was not remarkable.

The temperature was 101°F., and the pulse 110. There was no anemia. The white-cell count was 7100, with 55 per cent polymorphonuclear leukocytes, 37 per cent lymphocytes and 8 per cent monocytes. The urine and stool examinations were negative. A roentgenogram showed the heart and lungs to be normal. Two electrocardiograms were normal.

The patient received no specific therapy. The temperature and pulse fell to normal on the 3rd day after admission and did not rise again. The patient remained asymptomatic and was discharged on the 17th day.

A blood culture taken on the day of admission was positive for *S. oranienburg*. On October 23, the patient's serum agglutinated his own organism to a dilution of 1:1280. Stool cultures on October 24 and 28 were positive for *S. oranienburg*, whereas stool cultures on two subsequent days were negative. A culture of the urine and one of the bile on October 28 were both sterile.

Case 8. R. B., a 7-year-old boy, was admitted on April 8, 1941. Eight days previously he developed a sore throat, cough, fever, swollen "glands" in the neck and pain on swallowing. Two days later his left ear began to discharge. Several days later there was an onset of diarrhea, which persisted.

On examination the patient appeared acutely ill and moderately dehydrated, and had a slight cough. Both eardrums were full and injected. The pharynx was injected, and the tonsils were enlarged. There was evidence of pneumonia at the base of the right lung. The heart was normal. The abdomen was slightly distended. The liver and spleen were not palpable.

The temperature was 101.5°F., the pulse 124, and the respirations 22. The hemoglobin was 55 per cent (Sahli), and the red-cell count 4,120,000. The white-cell count was

16,400, with 90 per cent polymorphonuclear leukocytes and 10 per cent lymphocytes. Subsequent counts varied between 7800 and 10,000. The urine contained a heavy trace of albumin and many leukocytes in the sediment. A Type 33 pneumococcus was cultured from the sputum. A roentgenogram showed consolidation of the right middle lobe of the lung.

The patient was given 0.5 gm. of sulfathiazole every 4 hours for 3 days. The temperature fell to normal on the 2nd day and then rose again, reaching 104°F. on the 4th day. On the 5th day it returned to normal, where it remained. The physical signs of pneumonia and diarrhea disappeared by the 7th day. The diarrhea recurred on the 10th day and continued for 5 days. The urine consistently showed heavy traces of albumin, although there were no leukocytes in the urinary sediment after the 4th day. The plasma nonprotein nitrogen determination on the 7th day was 46 mg. per 100 cc.

A blood culture taken the day after admission yielded *S. oranienburg*. A culture on April 14 was sterile. Urine cultures on April 15 and 19 and May 5 did not yield this organism. *S. oranienburg* was recovered from stool specimens on April 10 and 15, but not from stool cultures on May 7 and 8. A throat culture on April 15 was negative for this organism. On April 15 and May 27 the patient's serum agglutinated his organism to a dilution of 1:160.

S. oranienburg is a rare pathogen. Kauffmann[18] isolated it from several healthy individuals and from the stools of 3 children with diarrhea. Rimpau and Steinert[19] isolated it repeatedly from the stools of a healthy carrier, whose serum did not agglutinate the organism. They also isolated this organism from the stool of a woman with acute gastroenteritis. This patient's serum was found to agglutinate her organism to a dilution of 1:200 when tested eight days after onset of illness.

S. oranienburg is a monophasic organism which has the somatic antigens VI and VII and the type-specific flagellar antigens *m* and *t*. As noted in Table 1, the selective fermentation reactions of this organism are identical with those of *S. paratyphi C*. If, however, we had carried out fermentation tests with Stern's glycerol medium and Bitter's rhamnose medium,[18] it would have been possible to make a differentiation, since *S. oranienburg* gives positive fermentation reactions on these two mediums, whereas *S. paratyphi C* yields negative reactions. With stock *S. suipestifer* serum, *S. oranienburg* gives a somatic (finely granular) type of agglutination. This is in accord with their common somatic antigens. The diphasic *S. suipestifer* (*S. cholerae-suis*) serum absorbed with the monophasic strain (*S. cholerae-suis*, var. *kunzendorf*) failed to agglutinate the two *S. oranienburg* strains. This is to be expected, since the two organisms have distinct flagellar antigens. When injected subcutaneously and intraperitoneally into mice, the two *S. oranienburg* strains proved lethal.

Summary

Six sporadic human cases of infection with *S. suipestifer* are described. Clinically these cases showed great variation. The bacteriologic identification of this organism and its separation into types are discussed. Two cases of *S. oranienburg* infection are described, and the close bacteriologic similarity of this organism with *S. suipestifer* is considered.

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RHEUMATOID ARTHRITIS AS A CAUSE OF INCREASED CEREBROSPINAL-FLUID PROTEIN*

A Study of One Hundred and One Patients

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THE neurologic manifestations of rheumatoid arthritis are numerous, extremely variable and at times so striking as to simulate disease of the central or peripheral nervous system. They comprise evidence of increased vasomotor activity, such as cold, clammy, cyanotic extremities, vasospasm, tachycardia and visual-field defects; sensory phenomena, including paresthesia, changes in sensory perception and referred radiating pains with radicular or segmental distribution; abnormalities of the motor system marked by muscular weakness, atrophy and hyperirritability, leading to tremor, twitchings, cramps and changes in the tendon reflexes; and possibly trophic changes of the skin, hair and nails. One or more such clinical features of the disease have been observed in 66 per cent of 293 unselected consecutive patients with rheumatoid arthritis. An analysis of these findings and the results of detailed neuropathological studies will be the subject of a future report.[1]

The present investigation, concerning the cerebrospinal-fluid findings in rheumatoid arthritis, was begun in 1935. In the meantime, Graber-Duvernay and Gerbay,[2] employing an inexact method for the determination of protein, reported an elevated cerebrospinal-fluid protein in 8 of 15 patients with moderate to severe rheumatoid arthritis, of whom only 1 had spondylitis. A little later, Marron,[3] using a tyrosine equivalent method for protein analysis, noted cerebrospinal-fluid proteins varying from 31 to 60 mg. per 100 cc. in 6 cases of arthritis of the spine, unspecified as to type. Except for these two papers, a search of the literature has failed to reveal any reference to the subject.

MATERIALS AND METHODS

The cerebrospinal fluids examined during the course of this study were obtained from 101 patients with rheumatoid arthritis, of whom 59 suffered from peripheral-joint disease alone and 42 from spondylitis, with or without peripheral-joint involvement. All were under our personal observation, many being in the group of 293 cases previously referred to. The diagnosis of spondylitis was based on stiffness, pain, tenderness, limitation of motion and deformity of the spine. There was frequently a history of sciatica or intercostal, segmental or pleuritic pain. Straight leg-raising was usually limited and often associated with some restriction of the motions of either the hips or shoulders or both. As a rule the chest expansion and vital capacity were markedly reduced. Increased knee and ankle jerks were commonly found, and an absent Achilles-tendon reflex (at the time the sciatica was present), meralgia paraesthetica and other neurologic abnormalities were demonstrable in some cases. Roentgenologic evidence of disease of the sacroiliac or spinal articulations was present in all but 1 of the spondylitis group, the exception being an early case with typical findings of rheumatoid spondylitis. All these patients had elevated sedimentation rates.

Since it was soon apparent that cerebrospinal-fluid abnormalities were encountered more frequently in the patients with spondylitis, we included more patients with this type of rheumatoid arthritis. As a result, the age and sex distributions of the cases studied and the ratio of one group to the other are not the same as they would be in an unselected consecutive series (Table 1). However, it will be seen from Table 2 that the distribution by duration and severity of disease is more nearly comparable to what one might expect to find in an unselected group of cases.

TABLE 1. *Distribution of Patients according to Age and Sex.*

AGE	WITHOUT SPONDYLITIS			WITH SPONDYLITIS		
	MALES	FEMALES	TOTAL	MALES	FEMALES	TOTAL
Under 20 yr.	5	6	11	5	0	5
20 to 39 yr.	5	20	25	23	5	28
40 to 59 yr.	5	15	20	7	2	9
60 yr. and over	2	1	3	0	0	0
Totals	17	42	59	35	7	42

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Cerebrospinal-fluid analyses* were repeated in 11 cases (7 with and 4 without spondylitis), with intervals ranging from two weeks to three years. The following chemical methods were used: sugar, Folin[4]; chloride, Wilson and Ball[5]; protein, Ayer, Dailey and Fremont-Smith[6]; colloidal-gold curve, Lange.[7] We have considered the following values as being characteristic of normal cerebrospinal fluid[8]: initial pressure, 70 to 180 mm. of water (pressures of 180 to 200 mm. and greater than 200 mm. are thought to be questionably abnormal and definitely increased respectively); leukocytes, 0 to 5 cells per cu. mm.; sugar, 50 to 100 mg. per 100 cc.; chlorides, 695 to 762 mg. per 100 cc.; protein, lumbar fluid, 15 to 45 mg. per 100 cc., and cistern fluid, 15 to 25 mg. per 100 cc.; colloidal-gold curve, no change greater than 2 in each tube.

TABLE 2. *Distribution of Patients according to Duration and Severity of Disease.*

	Duration			Severity		
	Under 1 yr.	1–5 yr.	Over 5 yr.	Mild	Moderate	Severe
Without spondylitis	14	29	16	14	25	20
With spondylitis	5	18	19	5	19	18
Totals	19	47	35	19	44	38

RESULTS

The initial pressure, measured in 93 cases, was normal in all but 7. In 5 it was questionably abnormal (in 1 case 195 mm. and in 4 cases 200 mm. of water), and in 2 it was definitely high (210 and 250 mm. of water). In only 1 of the latter was the protein content increased. In the absence of other abnormalities, these slightly increased initial pressures probably represent incomplete relaxation of the patient. Pleocytosis was present in 3 cases, but all the fluids were contaminated with blood in sufficient quantity to explain the increase in white cells. In 41 of 44 cases the sugar determinations were normal. The slight reductions observed in the other 3 cases (46.0, 48.0 and 48.5 mg. per 100 cc.) are not significant. The chloride determinations in only 3 of 34 cases were lower than normal (693, 690 and 670 mg. per 100 cc.). Minor reductions of this type, particularly when not accompanied by other changes, are of no diagnostic importance.[8] Similarly, we did not regard as significant total protein values of 12 to 14 mg. per 100 cc.[8] observed in fluids from 5 patients in the group with peripheral-joint involvement alone, 4 of whom were under eighteen years of age.

The number of patients having increased cerebrospinal-fluid proteins and abnormal colloidal-gold curves is shown in Table 3. It will be noted that the percentage of fluids showing an increased protein content was significantly higher in the spondylitis group than in the group with peripheral involvement alone, and that only a small proportion of the fluids gave an abnormal colloidal-gold curve.

TABLE 3. *Incidence of Increased Cerebrospinal-Fluid Protein Contents and Abnormal Colloidal-Gold Reactions in Patients without and with Spondylitis.*

Patients	Without Spondylitis				With Spondylitis				Percentage Difference
	Males	Females	Total		Males	Females	Total		
			No.	%			No.	%	
All examined	17	42	59		35	7	42		
Those with a high total protein	4	0	4	6.8	11	1	12	28.6	19.8 (±7.4)
Those with an abnormal colloidal-gold reaction	2	3	5	8.5	6	0	6	15.0	6.5 (±6.4)

The increased cerebrospinal-fluid protein contents observed in the individual patients without spondylitis are listed separately in Table 4. Fluids from 3 other patients in this group exhibited an increased colloidal-gold reaction but were otherwise normal; these curves are shown in Table 5.

TABLE 4. *Increased Cerebrospinal-Fluid Protein Contents and the Colloidal-Gold Reactions in Patients without Spondylitis.*

Date	Name of Patient	Sex	Age	Protein Content	Gold-Sol Curve	Type of Fluid
			yr.	mg./100 cc.		
4/13/35	J. R. W.	M	36	46	0000000000	Lumbar
4/8/36	B. D.	M	54	47	0012321100	Lumbar
11/10/35	W. S. D.	M	64	55	0000121100	Lumbar
3/7/36				25	0000000000	Lumbar
2/6/35	J. McI.	M	49	66	0001233310	Lumbar
3/1/35				70		Lumbar
				51		Dorsal
				40		Cistern

Thus it will be seen that only 9 of the 59 patients with rheumatoid arthritis involving the peripheral joints alone had spinal-fluid alterations, 4 having increased proteins, 2 (J. McI. and B. D.) with associated abnormal gold-sol curves, and 3 having only abnormalities of the gold-sol curve

*The cerebrospinal-fluid determinations were carried out in the Spinal Fluid Laboratory of the Massachusetts General Hospital by Miss Eulalia Gzebienowska and Mrs. Charles McCann, to whom we are indebted for their services.

The latter changes usually occurred in the first and middle zones. Lumbar punctures were repeated in 4 cases from this group. In 2, both fluids were normal. In patient J. McI., re-examination confirmed the finding of a previous high protein,

TABLE 5. *Abnormal Colloidal-Gold Reactions in Cerebrospinal Fluids without Increased Protein Content in Patients without Spondylitis.*

NAME OF PATIENT	SEX	AGE	PROTEIN CONTENT	GOLD-SOL CURVE
		yr.	*mg./100 cc.*	
L. S.	F	34	31	1123210000
S. K.	F	36	30	1233221000
R. R.	F	35	32	5555552100

but in patient W. S. D. the second fluid was normal. He entered the hospital complaining of acute rheumatoid arthritis and frequent nocturnal erections. Although the protein was elevated at that time, there was no evidence of neurologic disease. A urethral stricture was present and was thought

TABLE 6. *Increased Cerebrospinal-Fluid Protein Contents and the Colloidal-Gold Reactions in Patients with Spondylitis.*

DATE	NAME OF PATIENT	SEX	AGE	PROTEIN CONTENT	GOLD-SOL CURVE	TYPE OF FLUID
			yr.	*mg./100 cc.*		
6/14/39	F. M.	M	34	47	0001210000	Lumbar
6/13/41	E. A.	M	39	48	0011110000	Lumbar
5/9/40	H. E.	M	15	51	0012221000	Lumbar
5/16/40				25	0001111000	Lumbar
7/25/40				65	0122332100	Lumbar
6/25/40	A. McK.	M	23	53	0001110000	Lumbar
1/30/41				55	0011100000	Lumbar
1/27/41	A. L.	M	53	58	0122210000	Lumbar
2/1/40	J. dP.	M	27	60	5555533100	Lumbar
5/23/40				58	5555553110	Lumbar
11/29/40				51	5555553100	Lumbar
1/26/39	R. G.	M	21	60	0011221000	Lumbar
1/26/39				44		Lumbar
5/8/39				41	0011221000	Lumbar
3/28/41	H. O. D.	M	44	60		Lumbar
5/31/40	W. D.	M	33	80	0012211000	Lumbar
6/18/41	Q. M.	F	48	85		Lumbar
4/17/41	W. N. B.	M	26	103	0001222100	Lumbar
12/31/37	M. L. V.	M	41	105	0000122100	Lumbar
1/25/38				121	0001221000	Lumbar
1/25/38				31		Cistern

to explain the genital symptoms. Re-examination was made three years later, at a time when the arthritis was quiescent but the erections continued.

Increased cerebrospinal-fluid protein was found in 12 of the 42 patients having spondylitis. The values are given in Table 6. Two of these 12 patients (H. E. and J. dP.) and 4 others without associated high protein had abnormal gold-sol curves. The latter are shown in Table 7.

Of the 7 patients in the spondylitis group in whom the spinal fluid was examined on more than one occasion, 3 were consistently abnormal (high protein, with or without abnormal gold-sol curves), 2 were consistently normal except for a questionably abnormal initial pressure in 1, and 2 (R. G. and H. E.) showed a high protein content or an abnormal gold-sol curve on some occasions and were normal on others. (See Table 6.)

Thus it will be seen that 23 of the 101 patients had cerebrospinal-fluid alterations, 16 with increased protein contents, with or without accompanying increased colloidal-gold reactivity, and 7

TABLE 7. *Abnormal Colloidal-Gold Reactions in Cerebrospinal Fluids without Increased Protein Content in Patients with Spondylitis.*

NAME OF PATIENT	SEX	AGE	PROTEIN CONTENT	GOLD-SOL CURVE
		yr.	*mg./100 cc.*	
R. F.	M	32	20	5555211000
J. N.	M	36	29	4333211000
L. S.	M	35	29	1233310000
H. W.	M	58	40	1122321000

with abnormal colloidal-gold curves only. As previously noted, 12 of the 16 patients with elevated proteins had spondylitis. In view of this finding, it is of considerable interest that 3 of the 4 patients (all males) in the group with peripheral-joint involvement showing elevated proteins had clinical symptoms suggestive of spondylitis at the time of the lumbar puncture. A definite diagnosis of spondylitis was not justified at the time, but one of the patients (J. R. W.) developed roentgenologic changes in the sacroiliac articulations at a later date. The fact that 15 of the 16 patients with increased proteins had either spondylitis (12 cases) or symptoms indicative of spinal involvement (3 cases) strongly suggests a relation between an elevation of the cerebrospinal-fluid protein and the presence of rheumatoid arthritis in the spinal and sacroiliac articulations. In the 2 patients with high proteins in whom cistern punctures were also performed (J. McI. of the peripheral group and M. L. V. of the spondylitic group), the fluid also showed an elevation of protein (40 and 31 mg. per 100 cc., respectively), as did fluid taken simultaneously from the dorsal region in the case of J. McI.

No significant relation could be established between the level of the spinal-fluid protein and the age or sex of the patients with spinal involvement (except that spondylitis occurs predominantly in males), the duration or total severity of the disease or the sedimentation rate. Table 8 shows that severe pain or sciatica or both were much more frequent in the high-protein group, which suggests that these patients were suffering from more active disease.

Discussion

It is generally agreed that abnormal gold-sol curves are related to the cerebrospinal-fluid albumin-globulin ratio, the globulin fraction being more active in causing the reaction.[8–11] More recently, Kabat et al.,[11] employing the Tiselius electrophoresis apparatus, showed that in certain diseases all the colloidal-gold reactivity was found in the gamma globulin fraction and none in the albumin fraction. They stated, "Although the colloidal gold reacting material is found in the gamma fraction, it may differ from the normal gamma component of spinal fluid, since other fluids which contain equally large amounts of gamma globulin yield normal colloidal gold curves." They were also able to demonstrate that cerebrospinal-fluid proteins show a similar pattern to that of the serum proteins. Since it is known that the serum albumin-globulin ratio may be reversed in patients with rheumatoid arthritis, with or without elevation of the serum protein,[12–14] it seemed logical to suspect that the spinal-fluid protein and colloidal-gold curve abnormalities were a reflection of alterations in the serum proteins. The latter were determined in too small a number of cases to draw any definite conclusions. The data suggest, however, as shown in Table 9, that, *in cases with spondylitis*, abnormal gold-sol curves are related to elevation of the serum globulin. It is possible that these abnormalities are related, in part, to the types or concentrations of globulin in such cases.[11] However, it is more likely that changes in the total cerebrospinal-fluid protein or in the globulin (the latter resulting in abnormal gold-sol curves) are due chiefly to an increased permeability of the spinal-cord membranes as a result of their proximity to acutely inflamed articular tissues. The findings in Tables 8 and 9 are consistent with such a premise. That the increased permeability is greatest in the lumbar region is suggested by the diminishing protein content of fluids taken simultaneously from higher levels (the dorsal region and the cisterna magna). In these cases, the protein increase was not uniformly distributed through the subarachnoid space, as is the case in a metabolic disorder, such as myxedema.[8]

Table 8. *Incidence of Severe Pain and Sciatica in Spondylitis Patients with and without Increased Cerebrospinal-Fluid Protein Contents.*

Symptoms	Protein Content: Normal No.	Normal %	High No.	High %	Percentage Difference
Mild or moderate pain, without sciatica	23	86.7	3	25.0	
Severe pain or sciatica or both	7	23.3	9	75.0	61.7 (±16.6)
Totals	30		12		

Diagnostic Implications

The diagnosis of spondylitis, especially in early cases, may at times be extremely difficult. This is particularly true of patients *having an increased cerebrospinal-fluid protein*, complaining of back pain with sciatic radiation (increased by coughing and sneezing) and exhibiting flattening of the lumbar curve, diminution of motion of the lumbar spine and of straight leg-raising, and atrophy and weakness of the muscles of the thighs and legs. The neurologic examination is, as a rule, negative except for hyper-reflexia, although meralgia paraesthetica and an absent Achilles-tendon reflex are rarely observed. In such cases the diagnostic possibilities include ruptured intervertebral disk, intraspinal neoplasm, metastatic malignant disease, a thickened ligamentum flavum, arachnoiditis, subarachnoid hemorrhage following trauma, and rarely diabetic neuritis, syringomyelia and multiple sclerosis. It is not within the scope of this paper to discuss in detail the diagnosis of each of these conditions.

Table 9. *Relation between Abnormal Cerebrospinal-Fluid Protein Contents and Gold-Sol Curves and Serum Globulin.*

Type of Involvement	No. of Cases	Serum: Increased Protein	Serum: Increased Globulin	Cerebrospinal Fluid: Increased Protein	Cerebrospinal Fluid: Globulin Present	Cerebrospinal Fluid: Abnormal Gold-Sol Curve
Peripheral	4	0	0	0	No determination	0
	7	4	7	0	No determination	1
Spondylitic	3	0	0	0	No determination	0
	4	3	4	3	3	3

The presence of a ruptured intervertebral disk has been suspected in a number of the spondylitic patients in this series. Two of them (Q. M. and W. N. B.) had negative lipiodol reactions, and in 1 (Q. M.) a negative exploration of the spinal canal was carried out at another hospital because of a suspected ruptured intervertebral disk. The clinical differentiation should as a rule be relatively easy. In the case of a ruptured intervertebral disk, the onset is usually acute, and a history of injury is

present in about 80 per cent of cases,[15, 16] absent or diminished ankle jerks in 50 to 70 per cent,[15, 16] anesthesia or hypoesthesia of the leg or foot in 35 per cent[15, 16] and a positive lipiodol reaction in over 90 per cent.[15, 16] On the other hand, in patients with spondylitis the onset is insidious, a history of injury is infrequent, neurologic abnormalities are uncommon, and the lipiodol reaction is negative.

The diagnosis of rheumatoid arthritis of the spine is frequently missed because the examiner is not cognizant of its symptoms and signs. In fact, a careful history alone should often serve to differentiate rheumatoid spondylitis from a ruptured intervertebral disk. In addition to the symptomatology and signs of spondylitis previously mentioned, these patients frequently complain of pain in areas of the spine other than the lumbar and sacral regions. Their symptoms are always worse on awakening and associated with generalized stiffness. They rarely obtain relief on lying down. Most of them admit suffering from general malaise, easy fatigability, anorexia and weight loss, often preceding the onset of the articular symptoms. Finally, the characteristic roentgenographic changes in the sacroiliac joints (narrowing, irregularity, haziness, decalcification and increased bone formation, occurring alone or simultaneously and eventually leading to fusion) usually occur early in the disease. Occasionally, the history, physical findings, and cerebrospinal fluid and roentgenologic examinations are not sufficiently characteristic to allow one to make the diagnosis. In such cases only the passage of time will allow for progression of the disease and the establishment of the correct diagnosis.

Summary

The cerebrospinal fluids from 101 patients with rheumatoid arthritis, 42 having spondylitis with or without peripheral arthritis, and 59 having involvement of the peripheral joints alone, were examined.

The only significant abnormalities observed were increased protein contents, abnormal colloidal-gold curves or a combination of the two.

Nine, or 12 per cent, of the 59 patients with rheumatoid arthritis involving the peripheral joints alone and 16, or 38 per cent, of the 42 patients with spondylitis exhibited such abnormalities.

Fifteen of the 16 patients with increased cerebrospinal-fluid protein had either spondylitis or symptoms suggesting spinal involvement. This fact points strongly to a relation between an elevation of the spinal-fluid protein and the presence of rheumatoid arthritis in the spinal and sacroiliac articulations.

Cerebrospinal-fluid alterations occurred more frequently in the spondylitis patients with severe pain or sciatica or both and hence presumably with a higher degree of inflammatory activity.

Factors probably involved in the production of these abnormalities are alterations in the serum proteins and increased permeability of the meninges from their proximity to inflamed articular tissue.

Attention is called to the diagnostic difficulties presented by patients with rheumatoid spondylitis and increased cerebrospinal-fluid protein, with particular reference to their differentiation from cases with ruptured intervertebral disks.

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MEDICAL PROGRESS

THE MECHANISM OF HEART FAILURE AND RELATED STATES (concluded)*

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BOSTON

Circulatory Changes Subsequent to Treatment

It has already been brought out that as a result of the treatment of congestive failure with digitalis and other measures, the cardiac output usually improves, although not to the level that existed prior to failure. Harrison,[35] however, has emphasized that this improvement in volume flow is not invariable nor does it bear any close relation to the change in clinical symptomatology; and Starr[9] has published examples of improvement in heart failure accompanied by a decrease in output. Starr has also presented data obtained with the ballistocardiogram indicating that the initial dose of digitalis may produce a temporary increase in cardiac output greater than that which persists when the full digitalizing effect is obtained.

The well-known value of the application of multiple tourniquets in the treatment of acute pulmonary edema is given objective experimental confirmation in the studies of Ebert and Stead,[36] who show that the application of such tourniquets can result in a temporary diminution in the circulating blood volume averaging 720 cc., and that this measure is thus temporarily the equivalent of a good-sized venesection.

Certain changes observed with the onset of diuresis have been discussed in the previous section. Proger, Ginsburg and Magendantz,[37] Schroeder,[38] Schemm[39] and Ellis[40] have shown the value of restriction of sodium in the diet in controlling cardiac edema.

The rationale for weight reduction in heart disease receives confirmation in the work of Master et al.,[41] who have demonstrated that the oxygen consumption, cardiac output and cardiac work are diminished when overweight subjects undergo weight reduction. Proger and Magendantz[42] had previously shown a reduction in cardiac output and cardiac work of patients with congestive heart failure subjected to prolonged dietary restriction.

Subnormal Circulation and Neurocirculatory Asthenia

A clinical picture that has posed a problem to physicians is that of patients who complain of weakness, giddiness when upright, fainting and a host of related symptoms. Some such patients are chronically troubled by these complaints and are usually labeled as having neurocirculatory asthenia; in others the symptoms develop only during or after an acute infection or some other debilitating disease. It has long been recognized that in such patients the circulation is inadequate. Starr and Jonas[43] have recently shown by ballistocardiographic studies that many of these patients, together with many elderly people with arteriosclerosis, and patients with coronary disease and with heart block, have inadequate cardiac outputs. The diminution of cardiac output in many of these patients, especially those with neurocirculatory asthenia and the postinfectious group, is not necessarily on a cardiac basis, but may well be due to inadequate peripheral compensation and poor return of blood to the heart. Starr has, however, also demonstrated that some patients, likewise diagnosed as having neurocirculatory asthenia, whose symptoms are somewhat similar have normal or increased cardiac outputs, and he suggested a separation of the two types. The symptoms of the latter group in many ways resemble Graves's disease. They complain of nervousness, tachycardia, palpitation, dizziness and dyspnea on exertion. The underlying etiology of the disturbed circulation in patients with neurocirculatory asthenia is of course not clarified by these investigations. The disturbance is probably due to central autonomic nervous stimuli arising in patients who are constitutionally predisposed to react in this fashion when under strain.

Shock and Cardiac Failure

What in many ways is an extreme and acute aggravation of the type of symptoms previously described as exhibited by patients with a subnormal circulation is the clinical picture usually called shock or peripheral circulatory collapse — extreme weakness, stupor, sweating, cyanosis, cold extremities, drop in blood pressure and so forth. It is

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generally believed that this is essentially a phenomenon of disturbance of the peripheral circulation, with a disproportion between the capacity of the peripheral vascular bed and the circulating blood volume. Some recent work has indicated that in certain circumstances an element of heart failure may be involved. Ebert and Stead[44] have presented evidence that in the shock picture occurring terminally in overwhelming infections there is little or no diminution in plasma volume and the venous pressure is relatively well maintained, and they believe that injury of both the heart and the peripheral circulation is involved. The same authors[45] have also carried out studies suggesting that a similar shock syndrome occurring in patients with acute myocardial infarction or chronic congestive failure may be due to cardiac failure alone.

Wiggers and Werle[46] found that the heart as well as the peripheral circulation may be involved in experimental shock. They state:

> The capacity of the ventricles to respond to a given venous pressure is reduced, perhaps due to a prolonged reduction in coronary blood flow. The results strongly suggest that this is one of the factors which precipitate an irreversible circulatory state. Although the observations are limited to shock from a prolonged period of posthemorrhagic hypotension with reinfusion of blood, they nevertheless suggest that we may have accepted too hastily the theory that the myocardium is unimpaired in shock and that the course of circulatory failure cannot be benefited by the use of cardiac stimulants.

Circulatory Dynamics in Specific Types of Cardiovascular Disease

Fast and slow ventricular rates. Stewart and his co-workers[47] have shown that abnormal cardiac rhythms associated with fast ventricular rates, such as auricular fibrillation or flutter and supraventricular or ventricular tachycardia, are inefficient, leading to a decreased cardiac output per minute and per beat, dilatation of the heart and decrease in the amount of work done by it. On the other hand, slow ventricular rhythms, such as those that occur in high-grade heart block, are relatively efficient. Although the cardiac output per minute is somewhat reduced, the output per beat is greatly increased, the heart does not dilate, and the work accomplished is commensurate with the size of the heart.

Valvular heart disease. Stewart et al.[48] have made cardiodynamic studies that bear out the clinical impression long held regarding the degree of strain imposed on the heart by valvular lesions. Single lesions are not incompatible with normal function of the heart, but a combination of defects, such as mitral stenosis and insufficiency, is always, according to their observations, accompanied by reduction in function. Patients with mitral disease and aortic regurgitation show less functional impairment than do those with mitral involvement alone; in other words, aortic regurgitation is of functional benefit. Aortic stenosis in combination with other lesions always results in marked decrease in function.

Bazett, LaPlace and Scott[49] presented observations on 2 subjects with free aortic regurgitation in whom the amount of blood regurgitated was 16.6 and 31 per cent, respectively, of the total ejected by the left ventricle. The total output of the left ventricle in this condition is thus greatly elevated and its work may be increased by 50 per cent or more.

Adhesive pericarditis and pericardial effusion. Stewart et al[50] found that constrictive pericarditis results in a decrease in cardiac output and an elevation of venous pressure owing to interference with the inflow of blood to the right side of the heart and possible impairment of contraction. In another paper[51] they reported essentially similar results in pericardial effusions. In both conditions with removal of the tamponade the cardiodynamics returned to normal.

Congenital cardiovascular defects. An important study by Eppinger, Burwell and Gross[52] on 6 patients with uncomplicated patent ductus arteriosus brings out the astonishing fact that the amount of blood flowing through the patent ductus may be from 4 to 19 liters per minute, representing from 45 to 75 per cent of all the blood pumped by the left ventricle. The increased work load on the heart and especially on the left ventricle is obvious.

Stewart and Bailey[53] carried out measurements in 14 cases of coarctation of the aorta and found that the output of the heart was normal or even increased before the onset of failure. Because of the elevation of blood pressure in the aorta, the work of the left ventricle in these patients was increased. Nevertheless only 5 of the patients showed cardiac enlargement, and when this occurred the prognosis was poor. The nature of the hypertension in this condition has long been the subject of study and speculation. It has been held that it is neurogenic in nature,[54] but this has been denied (Pickering[55]). Recently, as the result of Goldblatt's demonstration that chronic hypertension may be produced experimentally by reduction in renal blood flow, the thesis has been advanced that coarctation of the aorta is in essence a "Goldblatt clamp" that reduces renal blood flow, and that this in turn releases a hormonal vasopressor mechanism. Evidence in favor of this belief is contributed by Friedman et al.,[56] who have

found a substantial reduction in renal blood flow in 6 patients with coarctation and by the experimental work of Rytand,[57] who obtained essentially similar results. If the hypertension of coarctation is similar to Goldblatt's experimental hypertension, one would expect a generalized vasoconstriction with increase in peripheral resistance, and not one limited to regions proximal to the aortic constriction. That this is indeed the case is suggested by the work of Steele,[58] who by direct measurements of intra-arterial pressure found that in the femoral arteries of such patients the diastolic pressures were elevated to an extent comparable to that in the arms, although the pulse pressures were unusually low.

Pulmonocardiac Failure

Although much attention has been paid in the Continental literature to "kyphoscoliotic heart disease," there has been comparatively little in English and American publications on this subject. Chapman, Dill and Graybiel,[59] however, have recently reported in detail the clinical and physiological features of this condition. Dyspnea, palpitation and fainting in patients with marked chest deformities are warning signs — signs unfortunately often mistakenly attributed to a neurosis. Although these patients may develop congestive failure of the usual type, this is unusual; sudden profound circulatory or respiratory collapse, frequently unresponsive to treatment, is common. The clinical state is different from that of the usual chronic cor pulmonale, or right-sided heart failure occurring in patients with chronic pulmonary disease such as emphysema, pulmonary fibrosis and so forth. The disturbed circulatory function in pulmonocardiac failure is dependent chiefly on interference with pulmonary dynamics — reduction in vital capacity, increase in residual air and inefficient pulmonary exchange of gases, with deficient arterial oxygenation, together with the great mechanical difficulty in respiratory movements.

Kerwin[60] reported 5 patients with pulmonocardiac failure in whom dyspnea and cyanosis were the most prominent clinical features. He pointed out what had been previously observed by Chapman, Dill and Graybiel and others, that hypertrophy and dilatation of the right side of the heart regularly occur, suggesting that chronic pulmonary hypertension had existed during life.

Summary

Recent investigations concerning alterations in circulatory physiology that occur in various types of heart disease and in heart failure are discussed especially as they bear on the explanation of clinical signs and symptoms. The numerous and complex factors concerned with the production and maintenance of clinical manifestations such as dyspnea or edema are brought out.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 29101

PRESENTATION OF CASE

A fifty-two-year-old man entered the hospital because of abdominal pain.

Approximately four years prior to admission the patient first suffered from attacks of crampy abdominal pain that were relieved by belching and cleared spontaneously after several weeks. He remained quite well until one year before entry, when he noted mild exertional dyspnea, which became worse six months later and was associated with easy fatigability. At that time he "strained his back" and was confined to bed for one month, when the back discomfort completely cleared. Six weeks before admission he began to suffer from attacks of lower abdominal crampy pain that extended across the abdomen, but apparently had no further radiation. Occasionally, the pain made the patient double up. The attacks usually lasted five to fifteen minutes and occurred irregularly during the day. There was no relation to meals but at times the pain occurred after fatty meals. There was no associated nausea, jaundice, fever or chills. Soda occasionally provided some relief and at times the pain was relieved by voiding. The bowels moved regularly, but the patient had taken a cathartic every day during the three weeks prior to admission. The stools were never bloody, tarry or acholic but at times were rather loose. Three weeks before entry his abdomen began to swell and he had some distress in the right upper quadrant, which had no apparent relation to the lower abdominal pain. This continued to the time of admission. Two weeks prior to admission, orthopnea developed and the patient required three pillows for rest in bed. No leg edema had been noticed. He then developed a cough that was productive of small amounts of yellowish sputum; there was no chest pain, but he did complain of a sense of fullness and aching at the costal margins. During the illness he had lost approximately 20 pounds. During the five years prior to admission, the patient's diet was irregular and of poor quantity and quality. He often missed two meals during a single day. He denied any more than "one drink a week."

The patient's mother died at seventy-four of "cancer," and his father died at seventy-six of "stoppage of the bowel." The past history was noncontributory.

Physical examination revealed a well-built man who had lost a great deal of weight. He belched frequently but appeared to be comfortable. The heart and lungs were normal. The abdomen was distended and tympanitic. No masses were felt, and no tenderness was elicited. A fluid wave was demonstrable. The inguinal lymph nodes on both sides were enlarged, firm, discrete, nontender and freely movable.

The blood pressure was 120 systolic, 80 diastolic. The temperature was 98.8°F., the pulse 90, and the respirations 20.

Examination of the blood revealed a hemoglobin of 13.2 gm. per 100 cc. and a white-cell count of 12,100. The urine was normal. The blood Hinton test was negative. The nonprotein nitrogen was 22 mg. per 100 cc., the chloride 97.7 milliequiv. per liter, and the protein 4.7 gm. per 100 cc. A flat plate of the abdomen demonstrated considerable air in a dilated stomach, but there was no evidence of dilated small or large bowel. There were numerous fine flecks of calcification that had the appearance of gall stones. The density of the abdomen was suggestive of fluid, but this may have been due in part to the patient's size. No air was seen within the biliary tree. A Graham test showed no filling of the gall bladder. There was dye in the stomach. A barium enema passed to the midsigmoid, where it met a complete obstruction. Insufficient barium passed the point of obstruction to demonstrate the type of lesion. There was considerable gas in slightly dilated loops of small bowel and in the descending colon.

An operation was performed on the third hospital day.

DIFFERENTIAL DIAGNOSIS

DR. EDWARD L. YOUNG: The exertional dyspnea and easy fatigability could indicate an old man getting older, or they could suggest the beginning of cardiac failure.

"There was no relation to meals but at times the pain occurred after fatty meals." This is a suggestion of gall-bladder trouble, as are the pains spoken of earlier that were relieved by belching. Gaseous distention of the stomach may cause pressure on a damaged gall bladder, and hence pain, which may be relieved by belching.

Although not at all diagnostic, the fact that soda relieved the pain is again of interest. If you ask a patient how and he says, "It makes me belch gas," that also makes you think of gall bladder. The

relief of ulcer pain by soda is a chemical rather than a mechanical relief.

In spite of the fact that we are taught in school to consider one diagnosis for the cause of symptoms, one has only to look at the diagnoses going out from this department to realize that all the patients we are dealing with have more than one anatomic lesion. This patient may have had gall stones and some other condition more recently.

The commonest cause of weight loss is cancer. The patient also had a suggestive family history.

On physical examination the patient belched frequently. Ninety-nine out of a 100 patients who sit down before you and belch will prove, if you watch them carefully, to be cribbers.

"The abdomen was distended and tympanitic." The one who reported that ought to have been more explicit. If it was tympanitic everywhere there was no fluid wave. Of course if he had said there was tympany in the midline, dullness in the flanks, and a fluid wave we might believe it; but the man was of good size, with a big belly, and had lost weight, and I defy anyone to be sure of a fluid wave under such conditions.

The enlarged lymph nodes are possibly important, probably not. The protein was below the so-called "edema level."

"No air was seen within the biliary tree." That is an interesting observation. It makes one think that the examiner was wondering about gallstone ileus. The only way I know of explaining air in the biliary tree is by a direct opening from the gall bladder into the intestine, which is also the only way a large gallstone gets into the intestine. Under these conditions we do occasionally see air in the biliary tree. Would you say that was so, Dr. Holmes?

Dr. George W. Holmes: Yes.

Dr. Young: We are not told about occult blood in the stool. Is that important? We are entitled to ask if there was enough coming from the bowel to test for occult blood. Of course we are given the strong suggestion that this man had gallstones. I am going to ask Dr. Holmes if he would be willing to be more explicit.

I do not believe we have any right to consider gallstone ileus on the basis of this story because the obstruction was in the midsigmoid. I have never known a gallstone to make trouble at that point. A gallstone can make trouble at various places in the small bowel, where it acts as an obturator. It often goes to the ileocecal valve and there makes trouble. Although the patient may have had gallstones, I do not believe they are the cause of his trouble.

In any man of this age coming in with a story of crampy pains and this appearance in the x-ray films, one first has to settle whether there is an obstruction that requires operation. Let us immediately say, "Yes." Then Dr. Mallory will ask what it was due to. The patient was fifty-two years old and may well have had malignant disease. That is always the first thing to consider. Malignant disease can fit this picture throughout — the crampy pains going on for a brief period beforehand, the slight loss of blood and the anemia.

What other things should one think of? We have thrown out gallstone ileus. I shall be arbitrary and say that it is not that. Could it be tuberculosis? The patient had questionable fluid in the belly. That either came from metastatic malignancy of the peritoneum or from tuberculosis. I doubt if it was tuberculosis for such lesions are commoner on the right side, in the region of the ileocecal valve. They do occur with some frequency on the left side, often enough so that we ought to consider tuberculosis. Diverticulitis could account for these symptoms but not for fluid in the peritoneal cavity. It could account for the white-cell count, which is slightly elevated, and a localized diverticulitis may have been the cause of the trouble, even though no diverticula were seen in the x-ray films. I cannot throw out the diagnosis completely.

What else is there? Intussusception gives a characteristic rectal discharge of mucus and prune-juice material; I believe that its absence rules out the diagnosis. Then there is the question of a large polypoid leiomyosarcoma, which is rare.

In other words this comes down to a question of obstruction due to malignant disease, diverticulitis or a combination of the two. Please remember that they can occur together. The important thing is what to do. There is one other thing we see about once a year in the hospital, namely, old people with merely a fecal impaction. We do a cecostomy, and when the smoke has cleared away we have nothing else to account for the difficulty. The thing to do here is to relieve the obstruction. Going merely on the theory of chances, I shall say that the cause was carcinoma of the sigmoid, with diverticulitis the second choice. It will not hurt my feelings to have it prove to be the second, but it will hurt my feelings to have it prove to be anything but one of these two. I should like Dr. Holmes to add anything he can from the x-ray films.

Dr. Holmes: There is positive evidence of gallstones, but there is nothing to make me think of gallstone ileus. In the first films there is little evidence of gas in the abdomen, and the more or less ground-glass appearance of the abdomen suggests the presence of a considerable amount of fluid. At no time was there an excessive amount

of gas in the small bowel. At one time the stomach was considered dilated with gas and there was more or less gas in the large bowel.

One thing of interest is that at no time was there much gas in the rectum.

DR. YOUNG: Was there loss of mucosa in the obstructed area?

DR. HOLMES: I do not believe so. I agree with the record: all that one can say is that the patient had obstruction. That is surprising. In diverticulitis or carcinoma, one can usually guess what the cause of the trouble is. These films, however, give no evidence other than that of obstruction.

DR. YOUNG: I might mention hernia, volvulus and other things, but I do not believe they deserve serious consideration.

DR. FLETCHER H. COLBY: I should like to ask Dr. Young if diverticula are apt to cause complete obstruction.

DR. YOUNG: No; but neither does cancer. There is generally a trickle to give a clue.

DR. HOLMES: That is true.

DR. REGINALD H. SMITHWICK: What is the level of the obstruction?

DR. HOLMES: It is near the rectosigmoidal junction.

DR. SMITHWICK: Do you think it is beneath the peritoneal inflection?

DR. HOLMES: I cannot answer that.

CLINICAL DIAGNOSES

Carcinoma of sigmoid.
Carcinomatosis peritonei.

DR. YOUNG'S DIAGNOSES

Carcinoma of sigmoid.
Carcinomatosis.

ANATOMICAL DIAGNOSES

Carcinoma of gall bladder, with regional metastases and diffuse peritoneal implantation.
Obstruction of sigmoid by adhesions.
Ascites.
Pulmonary edema.
Cholelithiasis.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: This patient was explored, and a presumably primary tumor was found in the region of the sigmoid. It was apparently thought that the degree of obstruction was not severe enough to necessitate a colostomy; so a specimen was taken and the surgeon backed out without doing anything more. The patient gradually accumulated more and more ascitic fluid, slowly failed and died.

Autopsy showed that the gallstones were directly connected with the intestinal obstruction but not in the form of gallstone ileus. The gall bladder contained many small stones, as Dr. Holmes pointed out, and one of the dangers of symptomless stones in the gall bladder is that they may induce carcinoma. There was a primary cancer of the gall bladder, a characteristic polypoid growth within the lumen of the organ. It had invaded the liver extensively and had metastasized to the lymph nodes around the head of the pancreas; at first there seemed to be cancer of the pancreas, but on dissection it became clear that the pancreas was surrounded by tumor but uninvolved. There were generalized peritoneal implantations, and these were most marked in the dependent portions of the abdomen. In the pelvis the cancer had grown in a diffuse sheet over the serosa of the sigmoid, anchoring it in the shape of a sharp S. The obstruction was due to the kinking rather than to anything else. The mucosa was uninvolved and it was quite possible to follow around the curves one at a time with an instrument, but functionally it was, as has been said, a fairly complete obstruction.

DR. YOUNG: How much fluid was in the belly?

DR. MALLORY: There were many encapsulated pockets of fluid, each quite separate from the other.

DR. YOUNG: Was this a separate tumor in the sigmoid or was it a metastatic tumor from the gall bladder?

DR. MALLORY: It was a peritoneal metastasis from the tumor in the gall bladder.

A PHYSICIAN: How about the lungs?

DR. MALLORY: They showed massive pulmonary edema, which was, I am sure, a terminal complication. The heart was normal.

DR. HOLMES: Was this man peritoneoscoped?

DR. MALLORY: No.

CASE 29102

PRESENTATION OF CASE

A forty-six-year-old Greek machinist entered the hospital because of swelling of the abdomen.

Six months prior to admission the patient noticed the onset of ankle edema. This became progressively worse, and three weeks before entry his abdomen began to swell. At that time he lost his appetite, felt nauseated and frequently vomited everything that he ate. His family noticed that he had lost his ruddy color and seemed yellow. This color deepened during the second week of his

illness but during the week prior to admission it began to fade. During the three weeks before entry he had had diarrhea four or five times a day, usually after eating, and his stools were described as yellowish but never clay colored. His diet was limited to milk and soups during this period. He developed an irritating nonproductive cough, and dyspnea requiring two pillows at night. The urine became dark, but this was unassociated with urinary symptoms other than nocturia (four or five times), which he had had for a year. Pain was not a prominent feature of the illness, but three weeks before entry he experienced a vague discomfort in the right back. During the next week he had occasional attacks of knifelike pain radiating from both flanks to the umbilicus, and later he had upper abdominal pain that radiated around to the back on both sides. The longest attack lasted two hours.

The patient consumed only a "moderate" amount of alcohol, and more than a jigger or two daily. There was no history of exposure to industrial solvents.

The family and past histories were noncontributory.

Physical examination disclosed a thin man who was not in obvious distress despite a markedly distended abdomen. The skin was dark and sallow. The scleras were yellow tinged. The diaphragm was high, particularly on the right. There were scattered crackling inspiratory rales at both bases of the lungs. Examination of the heart was negative. The abdomen was markedly distended and tense. A fluid wave was easily demonstrated and there was shifting dullness in both flanks. The liver edge was palpable 7 cm. below the costal border, and the edge was smooth. There was pitting edema of both lower extremities to the knees.

The blood pressure was 110 systolic, 70 diastolic. The temperature was 99°F., the pulse 100, and the respirations 22.

Examination of the blood revealed a red-cell count of 6,400,000 with a hemoglobin of 90 per cent, and a white-cell count of 6000, with 81 per cent polymorphonuclear leukocytes. The urine was acid in reaction, had a specific gravity of 1.024 and showed a ++ test for bile; the sediment contained 8 to 10 white cells per high-power field. The blood Hinton test was negative. One stool gave a +++ guaiac test, but two later examinations were negative. The van den Bergh was 3.8 mg. per 100 cc., direct, and 6.2 mg., indirect. The serum nonprotein nitrogen was 22 mg. per 100 cc., the chloride 97.7 milliequiv. per liter, and the protein 8.1 gm., the albumin 2.3 gm. and the globulin 5.8 gm. per 100 cc., making an albumin-globulin ratio of 0.4. The prothrombin time was 32 seconds (normal, 20 seconds). The cephalin flocculation test was ++ at 24°C. and ++++ at 40°C. A barium meal of the upper gastrointestinal tract showed marked curling of the lower esophagus; this area was slightly irritable and regurgitation occurred. A hiatus hernia measuring 2 by 2 cm. in diameter was seen, but there was no evidence of varices. The stomach was not remarkable. The duodenum and small intestines appeared normal so far as seen; however, examination was handicapped by the large amount of ascites. A barium enema passed from the rectum to the cecum without delay. There was no evidence of intrinsic disease in the rectum and colon. There appeared to be some depression or displacement of the sigmoid inferiorly, and the ascending and descending colon lay well laterally. No soft-tissue mass was demonstrated.

In spite of supportive treatment and paracentesis the patient failed rapidly. He became unable to retain any food or fluids. A flat plate of the abdomen after paracentesis demonstrated a markedly enlarged spleen. The lower aspect was not visible because of overlying intestinal gas. However, it reached almost to the level of the iliac bone. The shadow of the liver was apparently not enlarged. The patient died on the thirteenth day after admission.

Differential Diagnosis

Dr. Reed Harwood: I am sorry there is no roentgenologist here. "Curling" of the esophagus is supposedly due to adhesions and is of no particular significance except that it may sometimes be confused with esophageal varices. Esophageal varices were not demonstrated in this case. I should like to ask if the spleen was palpated after paracentesis, and if it did reach down as far as the iliac bone. The record indicates that the spleen was enormous, yet I see the iliac crest here and what I take to be the lower border of the spleen lies considerably above it. Would you agree with me, Dr. Jones, that the spleen is large but not enormous?

Dr. Chester Jones: The stomach shadow appears to be pushed over to the midline. It is hard to be sure, but I should agree that the shadow you indicate is probably spleen. There was so much fluid in the abdomen when that film was taken that many outlines are obscured.

Dr. Harwood: Another question I should ask the roentgenologist is, Do you think the spleen has pushed the descending colon laterally?

Dr. Chester Jones: It does not show it in this film.

Dr. Harwood: I should like to know how the roentgenologist interprets a finding of that sort. It may be significant.

DR. JONES: The two flexures seem to be in about the same position.

DR. HARWOOD: With you as my roentgenologist, Dr. Jones, I am going to take the liberty of discounting the statement that the descending colon was pushed laterally.

In summary we have the case of a patient who had edema, ascites, marked splenomegaly, jaundice, an inverted albumin-globulin ratio and a positive flocculation test. All these point strongly to severe liver damage. My first thought on reading the case over was that the patient had cirrhosis with a rapid progression, perhaps a toxic hepatitis. There are several points that are not entirely consistent with this diagnosis and I shall discuss these at some length.

The spleen, at least according to the interpretation of the X-ray Department, was unusually large for a case of alcoholic cirrhosis. As I read the record, it reminded me of the type of spleen one gets in Banti's disease. However, Banti's disease is a chronic ailment associated with marked anemia, and usually appears in people considerably younger than this man. Then again the jaundice is rather too marked for the ordinary case of alcoholic cirrhosis. However, in a case that is progressing rapidly with marked liver damage, jaundice of this degree could be expected to appear. Then we find that there were no esophageal varices. In alcoholic cirrhosis with a severe degree of ascites and a large spleen one would expect also to find esophageal varices. In addition, the history does not give us the usual immoderate intake of alcohol. However, many cases of cirrhosis in which the alcoholic intake was slight have been presented in this room.

The high serum protein is disturbing. In cirrhosis and most liver diseases the serum protein tends to be low, both the albumin and globulin being diminished, but the albumin to a greater extent. We are taught to think at once of multiple myeloma when we see a high serum protein. Multiple myeloma occasionally involves the spleen. However, I do not know of any cases in which ascites and jaundice were also present, so I am inclined to say this patient did not have multiple myeloma.

I am told that in the early stages of cirrhosis of the liver the serum globulin can be high and that only in the later stages does it become lowered, so this finding may be confirmatory evidence of the diagnosis of cirrhosis. The interval between the onset of the ascites and death is rather short for the usual case of chronic alcoholic cirrhosis. However, cases can progress as rapidly as this. Finally there is a high red-cell count (6,400,000) and a hemoglobin of 90 per cent. These are distinctly unusual findings in cirrhosis of the liver, in which anemia is the rule. It may be the clue to the diagnosis. I should like to ask Dr. Mallory if that was repeated and still found to be high.

DR. TRACY B. MALLORY: It was done on only one occasion.

DR. HARWOOD: Perhaps I should not put too much emphasis on that point. It is possible that the patient was dehydrated and had a certain degree of hemoconcentration as a result of his inability to take fluid and as a result of his diarrhea.

The record states that the patient had a ruddy color. Ruddy color and a high red-cell count, with a spleen that seemed rather larger than one would ordinarily expect in cirrhosis, make one think seriously of the diagnosis of polycythemia vera. We know that, in polycythemia vera, thromboses in various vessels are of common occurrence, particularly in the mesenteric vessels. I have not actually heard of a case of portal thrombosis in polycythemia, but at least it is conceivable that this man had portal thrombosis of gradual onset and progression, resulting in ascites, liver damage and death. The main objection is that in portal thrombosis the signs of ascites are also accompanied by marked hematemesis and even more rapid progression than in this case. Another objection to the diagnosis of polycythemia is that the red count was not extremely high. I should feel that I was on surer ground if the red-cell count had been 8,000,000 or 9,000,000. Finally, the patient did not have any of the other signs of polycythemia, such as cyanosis, distended veins and so forth. In any event I think it is a possibility. Other conditions, such as lymphoma and carcinoma of the liver, I have also thought of and discarded, because most of the signs seem to point toward a toxic hepatitis, and I shall make that my final diagnosis and just raise the question of the possibility of polycythemia with thrombosis of the portal vein.

DR. WILLIAM B. BREED: The absence of a roentgenologist gives us a golden opportunity to talk freely about these x-ray plates. I am not convinced that these pictures show merely "curling" of the lower end of the esophagus, and I should like to have someone convince me that this does not represent varices of the lower part of the esophagus. I have had occasion to review similar pictures with the roentgenologist and from time to time have persuaded him to reverse the decision. Can anyone discuss this a little more intelligently than I can? Dr. Jones, what do you think about it? How often do you see "curling" of the lower end of the esophagus? It seems an inadequate term and it does not look like curling to me. Would you say definitely that there were no varices?

DR. JONES: In the left-hand film there is "curling" and no suggestion of varices. In the third film to the right there is a slight suggestion of varices. It is sometimes possible by turning the patient to bring out a change in the esophageal contour. We find varices in about 40 to 50 per cent of our cases of cirrhosis. I am sure that the absence of demonstrable varices does not rule out cirrhosis of the liver. I think at times it is important diagnostically for a roentgenologist to say there are or are not varices. The right-hand film certainly shows something suggestive of varices.

DR. EDWARD B. BENEDICT: Extensive varices give filling defects.

DR. BREED: I acknowledge that they are not extensive, but I should like to give Dr. Harwood support.

DR. JONES: He certainly has enough evidence of intrahepatic involvement from the laboratory point of view. Whether that is the whole picture, I do not know.

DR. JOSEPH AUB: I am beguiled by the high globulin. It is a rare finding and I wonder if sarcoid should be considered.

DR. JONES: I should say that hyperglobulinemia is rather the rule in liver disease, and that low serum protein is not necessarily the rule. I have recently looked up 50 cases of cirrhosis; most of the patients showed a normal total protein, and the normal figure was usually due to a high globulin. Therefore the serum protein figure by itself is not too significant. It is the albumin-globulin ratio that is important. Certainly, in the vast majority of patients with cirrhosis of the liver, if there is ascites or edema, there is an elevated globulin and an inverted ratio.

DR. MALLORY: A few months ago we had a meeting to discuss the possibility of eliminating unnecessary laboratory tests, and the question came up whether it was worth while to do albumin-globulin ratios. Dr. Butler was inclined to think they were rarely significant. Would you defend that statement, Dr. Butler?

DR. ALLAN M. BUTLER: I can attempt to. But before defending it, I should like to ask one question. I notice that this patient was a Greek, and I remember Dr. John Homans presenting a Greek patient, and saying that whenever you have such a patient remember he may have lived in Greece and may have come in contact with dogs and sheep. This fellow obviously had liver disease and a high globulin, and I wonder if he had lived in Greece and whether we should be thinking of echinococcal disease.

DR. MALLORY: He was born in Greece. There is no statement concerning how long he had been in this country.

DR. BUTLER: Now to defend the statement about determining albumin-globulin ratios for the duration of the war.

The albumin-globulin ratio is really only a qualitative analysis. Howe,* in 1921, said that 22 per cent of sodium sulfate precipitates the globulin and leaves the albumin in solution. Actually, when you precipitate any protein by increasing the salt concentration you get a logarithmic curve. If you take serum globulin and run a precipitation curve with increasing concentrations of sodium sulfate you find that with a concentration of 22 per cent all the globulin has not been precipitated. So at that particular sulfate concentration you have only a qualitative separation of albumin and globulin as some globulin remains in solution with the albumin. The next thing that makes it qualitative is that the sodium sulfate is supersaturated at room temperature. You have to keep the reagent in an incubator at 37°C. to keep the salt in solution. When the technician pipettes the sulfate solution at room temperature, sodium sulfate in varying amount crystallizes out on the pipette. The amount varies a great deal with the care of the particular technician. Thus unless analyses are done carefully there is a technical error as well as a theoretical error. These factors limit the value of the routine determination of albumin-globulin ratios.

Concerning the diagnosis, I think we all know that this patient had liver disease, even without the albumin-globulin ratio. If any patient has liver disease and has edema too, we can guess that he has a low albumin and maybe has a low total serum protein. This latter can be determined accurately by one of several simple procedures. If the serum protein is high and edema is present, we know that the albumin is low. We do not need to do an albumin determination. Thus in such a case the albumin-globulin ratio does not help a great deal. However, it may help in the rare case when one does not know whether the liver disease is serious. There was a girl presented at medical rounds six week ago who, from her story, might have had ordinary catarrhal jaundice. The albumin-globulin ratio, however, was 0.2. That provided one of the pieces of evidence that led us to believe that the girl had something more serious than catarrhal jaundice. I do not know what happened. Do you, Dr. Jones?

DR. JONES: She is still critically ill.

DR. BUTLER: In that case the albumin-globulin ratio was an important factor in appreciating the seriousness of the illness. There are such rare cases in which the ratio is helpful. But to turn around and do a ratio on every patient who has

*Howe, P. E. Use of sodium sulfate as globulin precipitant in determination of proteins in blood. *J. Biol. Chem.* 49:93-107, 1921.

liver disease and ascites, or on every nephritic patient who has albumin in the urine, is not helpful enough to justify the analysis at a time like the present when we are trying to cut down laboratory work.

DR. JONES: I am in accord with Dr. Butler. In almost every case of liver disease the diagnosis is made first and the laboratory test subsequently. I think there is justification for doing this test for prognostic purposes.

CLINICAL DIAGNOSES

Toxic cirrhosis.
Hepatoma?

DR. HARWOOD'S DIAGNOSES

Alcoholic cirrhosis.
Toxic hepatitis.
Polycythemia and portal thrombosis?

ANATOMICAL DIAGNOSES

Cirrhosis of liver, type undetermined.
Hepatoma.

PATHOLOGICAL DISCUSSION

DR. MALLORY: There is a rare type of case in which one must decide whether ascites is due to portal obstruction or to caval obstruction. In such cases the albumin-globulin ratio may be an important differential point.

This patient was peritoneoscoped by Dr. Benedict, who found a cirrhosis of unusual nodularity. Some of the nodules were a little peculiar in color and appearance so that Dr. Benedict suspected the possibility of tumor; however, he was unable to make a definite diagnosis. A biopsy of one of the nodules showed a hepatoma. Not long ago we had another case of hepatoma which had grown up the hepatic vein, as this tumor characteristically does, to form a tumor thrombus in the cava. In that man there was severe ascites in spite of a normal serum protein and a nearly normal albumin-globulin ratio. I thought the presence of a normal albumin-globulin ratio might have led one to suspect caval thrombosis by pointing toward a mechanical reason for the anasarca. In this case we have no evidence whether or not the cava was obstructed.

DR. HARWOOD: Were there any esophageal varices?

DR. MALLORY: We do not know; permission for an autopsy was not obtained.

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MENINGOCOCCAL INFECTIONS

Since cerebrospinal fever was first recognized in 1805 this disease has been known to occur almost constantly in a sporadic form and has assumed epidemic proportions at irregular intervals. It has flourished particularly during wartime both in the military and in the civilian population. Unlike such diseases as influenza, the outbreaks of meningitis are not explosive in their appearance and do not affect a large number of people. Rather, they begin insidiously, usually increase gradually and persist for several months and often for years, but never have a high attack rate. In England during World War I there were 300 cases in 1914, 2343 cases in 1915, 1278 cases in 1916 and 1385 cases in 1917. The case fatality rate during these years averaged about 65 per cent. In the United States Army during these years there were 5939 cases, with a mortality of about 40 per cent.

The present war has seen an even greater increase in the number of cases of this disease in Britain, where a total of 12,500 cases occurred during 1940. There has also been a marked increase in the occurrence of this disease in Canada, particularly in Nova Scotia, and, more recently, many cases have been reported in this country, particularly in New England and in neighboring states. Even greater numbers of cases are to be expected in the near future.

Compared with previous outbreaks, the present one shows several striking differences, which should be borne in mind in view of the serious attitude that health officers and the general population assume toward this disease. In addition to the low incidence of meningococcal meningitis both in the general population and among the military personnel, the case fatality rate is now surprisingly low. In Britain less than 10 per cent of all the cases occurring in the general population end fatally. In most large series of cases that have been reported, particularly those derived mainly from military sources, the mortality is more nearly 5 per cent. Young infants and aged persons still account for the greatest number of the deaths among civilians. In this country it is to be expected that less than 3 per cent of the cases occurring in army camps and less than 10 per cent of those occurring among the civil population will end fatally.

The great difference in mortality is, of course, due to the marked effectiveness of the sulfonamide drugs. Sulfadiazine is now usually recommended as the drug of choice but any of the other widely accepted sulfonamides, namely, sulfanilamide, sulfapyridine and sulfathiazole, are also effective. For the most favorable results these drugs must be given as early as possible in the course of the infection. In severe cases, particularly those in which the patient is already stuporous or unconscious, the first doses of drug should be given

parenterally. It may not be amiss, also, to emphasize the importance of the administration of fluids early in such cases since the dehydration resulting from lack of fluid intake and from vomiting may predispose to renal complications if the sulfonamide derivatives are given intravenously. Early diagnosis and early and intensive treatment are therefore highly important.

Another encouraging feature of the cases that have occurred recently is the almost complete absence of serious crippling complications in patients who are properly treated. This is in striking contrast to the high incidence of total deafness and blindness among those who survived attacks of cerebrospinal fever in previous outbreaks.

Finally, the present-day treatment is much simpler than before.* Lumbar puncture is now performed only for diagnosis or for the evaluation of the progress of therapy. Intraspinal injections of serum, with the severe complications resulting from their use, have now been completely and, it is hoped, permanently abandoned. Antimeningococcus serums, if given at all, are used only intravenously or intramuscularly in severe cases or when the disease fails to respond to chemotherapy alone. Most British physicians have completely abandoned the use of serums, but this may be due, in large measure, to expediency as well as to the excellent results obtained without them.

Several epidemiologic features are worth stressing. During periods when cases of meningococcal meningitis are prevalent there are numerous carriers of epidemic strains, particularly among the exposed population. In closed units, as in military barracks or even larger outfits, as many as 50 or even 75 per cent of persons may harbor meningococci in the nasopharynx without apparent infection. The factors underlying susceptibility to infection are not known.

There are, however, cases of meningococcemia without meningitis, which should be recognized and treated early since, if they remain untreated, the patients may develop meningitis. Such cases are, of course, most prevalent in epidemic periods. All persons having unexplained chills, petechial or purpuric rashes and joint pains or swellings accompanied by intermittent fever and headache should be suspected of having meningococcal infections. In some cases the symptoms are entirely respiratory and nowadays are likely to be attributed to atypical or virus pneumonia. Whenever possible, blood cultures should be made during the febrile phase and sulfonamide therapy should be given early.

During every epidemic there are a small percentage of severe and fulminating cases, usually with extensive purpuric eruptions. Some of these patients, today, fail to respond to intensive therapy. Such cases will probably comprise most of the deaths unless new methods are discovered for treating these patients more effectively.

With regard to prophylaxis, there seems little reason to advocate any large-scale adventures in this field. In small, compact and self-contained military units where action is anticipated soon after a case appears or after a large number of carriers are discovered it may be possible to eliminate the carrier state by a short course of sulfonamide therapy. Such a procedure at present is neither warranted nor feasible for large units of the population.

It is most important to emphasize the early recognition of cases of meningitis and of the various forms of meningococcal infection in the absence of meningitis and to treat such patients early.

*Dingle, J. H., and Finland, M. Diagnosis, treatment and prevention of meningococcic meningitis: with a résumé of practical aspects of treatment of other acute bacterial meningitides. *War Med.* 2:1-58, 1942.

FLORENCE CRITTENTON LEAGUE

The Florence Crittenton Mission, a national organization, was established sixty years ago to provide medical care and helpful guidance to the illegitimately pregnant woman, in an effort to protect society and the individual from the spread of immorality and disease. In the ensuing years "homes" have been established in sixty American cities. The Florence Crittenton League, the local chapter and the only one in New England, was founded fifty years ago. It consists of twenty-three

"circles" in and about Boston, whose members not only raise funds for the work of the League but also take an active interest in helping the girls or young women who come under its care.

The League maintains a home and hospital in Brighton, which is described in more detail elsewhere in this issue of the *Journal*, as well as Welcome House, a protective home for girls from fourteen to sixteen years of age who have been exposed to unwholesome environments.

The phenomenon of illegitimacy is not new, nor is it confined to any race or clime. It has been recognized as both a medical and a social problem for innumerable years and has been studied from all angles by experts in many fields, but no complete solution has yet been found. Although war, curiously, has not increased the burden of the Florence Crittenton homes, proper care of the girl who must bear the burden of illegitimate motherhood still remains a problem, and all physicians should be aware of the fact that this type of assistance can be obtained in Boston and many other parts of the country.

MEDICAL EPONYM

Swift–Ellis Treatment

This was described by Homer W. Swift (b. 1881) and Arthur W. M. Ellis (b. 1883) of the Rockefeller Institute for Medical Research, in the *New York Medical Journal* **96**: 53-55, 1912.

> Our method is to withdraw blood after intravenous injections of salvarsan or neosalvarsan, separate the serum, and on the following day dilute it to 40 per cent with normal saline. It is then heated at 56°C. for one-half hour. By means of lumbar puncture, 15 cc. of spinal fluid is withdrawn and then 30 cc. of the diluted serum, warmed to body temperature, is slowly injected into the subarachnoid space. The foot of the bed is raised for about an hour after the treatment.

R. W. B.

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Eliot Hubbard, Jr., M.D., *Treasurer* Pro Tem.

COMMITTEE ON MATERNAL WELFARE

Breech Delivery: Death caused by transection of spinal cord

Baby B. was born to a twenty-nine-year-old primipara at full term. Labor lasted fifteen hours and terminated in a breech delivery; although details are not available, this was said to have been "easy and noninstrumental." The birth weight was 6 pounds, 2 ounces. No asphyxia or cyanosis was noted, but the infant did not move its legs and the arms were limp. The left arm regained some motion; the right remained completely flaccid. At four days there seemed to be some movement of the legs, which was thought to be voluntary. On the seventh day, a consultant noted tension of the fontanel and obtained bright blood by lumbar puncture. On the next day the child was transferred to another hospital.

On admission the infant had regained its birth weight, but was cold, apathetic and dribbling small amounts of urine and feces. The right arm was flaccid, and the left was held in partial flexion and internal rotation. The legs were slightly contracted at the knees without voluntary motion, but with automatic mass withdrawal on stimulus to the skin anywhere on their surface. Active knee jerks were obtained. No evidence of pain on pinpoint stimulus was elicited anywhere below the neck, although usually such stimulus produced mass withdrawal of the legs. A slight facial asymmetry suggested paralysis on the right.

Two lumbar punctures during the week after admission produced grossly bloody fluid, which was thought to be due to trauma during the puncture. X-ray films of the spine showed no abnormality. It was thought that the infant had an injury to the spinal cord due to avulsion of the nerves of the right brachial plexus, with more or less complete transection of cord at the mid-cervical level. At first the child's temperature was distinctly subnormal; it then tended to rise and became irregular as aspiration of food and mucus, with resultant respiratory difficulty, increased. No changes occurred in the general neurologic picture, and the baby died eight weeks after birth, presumably because of aspiration pneumonia.

This cause of death was substantiated by autopsy, as was the neurologic lesion. There was avulsion of all the roots of the right brachial plexus,

with diffuse and practically complete transection of the spinal cord at the midcervical level. This injury was accompanied by a hemorrhagic infiltration of the distal portion of the cord, extravasated blood being found in decreasing amounts down to the level of the dorsal cord. No gross lesion of the brain or of its supporting structures or vascular supply was encountered.

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ALLERS, OLGA E., 28 Wellesley Avenue, Wellesley.
Woman's Medical College of Pennsylvania, 1938.

AVERY, BENNETT F., 41 Allerton Street, Brookline.
University of Michigan Medical School, 1926.

BURNS, FRANCIS A., 84 Central Street, Foxboro.
Middlesex University School of Medicine, 1934. Sponsor: Thomas H. O'Toole, 11 Walpole Street, Norwood.

CURRIER, WILBER D., 17 Seaver Street, Brookline.
University of Nebraska College of Medicine, 1938.

ELLIOT, HOWARD L., 14 Strathmore Road, Brookline.
McGill University Faculty of Medicine, 1929.

EPSTEIN, IDA F., 275 Normandy Street, Roxbury.
New York Medical College, 1937.

MCKELL, DAVID M., JR., 94 Longwood Avenue, Brookline.
Harvard Medical School, 1938.

SELIGMAN, ARNOLD M., 169 Rawson Road, Brookline.
Harvard Medical School, 1939.

SHALETT, IRVING J., 1589 Beacon Street, Brookline.
Middlesex University School of Medicine, 1928. Sponsor: Louis F. Curran, 409 Marlboro Street, Boston.

STOWELL, JOSEPH M., 10 Conant Road, Chestnut Hill.
Tufts College Medical School, 1936.

TANSEY, JOSEPH L., 63 Orchard Hill Road, Jamaica Plain.
Harvard Medical School, 1937.

VANDAM, LEROY D., 235 Park Drive, Boston.
New York University College of Medicine, 1938.

Timothy F. P. Lyons, *Secretary*
270 Commonwealth Avenue, Boston

NORFOLK SOUTH DISTRICT

ANGELO, PETER J., 229 Washington Street, Quincy.
Tufts College Medical School, 1941.

HOWLEY, EDWARD J., 39 Riley Avenue, East Weymouth.
Tufts College Medical School, 1941.

RUBIN, FRANK F., 795 Southern Artery, Quincy.
Middlesex University School of Medicine, 1936. Sponsor: George D. Dalton, 754 Hancock Street, Quincy.

Robert L. Cook, *Secretary*
38 Russell Park, Quincy

SUFFOLK DISTRICT

ASSAD, FREDERIC C., 1 Bond Street, Boston.
Middlesex University School of Medicine, 1934. Sponsor: Christus A. Pattajo, 10 Hollis Street, Boston.

BUTTS, VINCENT, 244 Meridian Street, East Boston.
College of Physicians and Surgeons, Boston, 1929. Sponsor: G. Lynde Gately, 624 Bennington Street, East Boston.

GIANTURCO, NICHOLAS D., 149 Hawthorne Street, Chelsea.
Middlesex University School of Medicine, 1934. Sponsor: Lamar Soutter, 266 Beacon Street, Boston.

GILBERT, RAYMOND E., 850 St. Marks Avenue, Brooklyn, New York.
Middlesex University School of Medicine, 1922. Sponsor: Russell F. Sheldon, 31 Pinckney Street, Boston.

GORDON, ROBERT K., 44 Winthrop Street, Winthrop.
Middlesex University School of Medicine, 1935. Sponsor: Earle M. Chapman, 266 Beacon Street, Boston.

HINDLE, WILLIAM V., 32 Queensberry Street, Boston.
Harvard Medical School, 1937.

HITE, JACOB W., 51 Park Drive, Boston.
Middlesex University School of Medicine, 1930. Sponsor: Louis E. Wolfson, 113 Bay State Road, Boston.

INGERSOLL, FRANCIS M., 2 Poplar Place, Boston.
Harvard Medical School, 1938.

KARP, ISADORE A., 153 Shurtleff Street, Chelsea.
Middlesex University School of Medicine, 1936. Sponsor: Frederick Ornsteen, 131 Washington Avenue, Chelsea.

LIEBMAN, SUMNER D., 122 Riverway, Boston.
Harvard Medical School, 1938.

RAMMELKAMP, CHARLES H., 66 East Newton Street, Boston.
The School of Medicine of the Division of the Biological Sciences, University of Chicago, 1936.

ROIFF, HARRY S., 159 Shurtleff Street, Chelsea.
St. Louis College of Physicians and Surgeons, 1923. Sponsor: H. Archer Berman, 475 Commonwealth Avenue, Boston.

SAFFRAN, IRVING, Fort Lewis, Washington.
Middlesex University School of Medicine, 1937. Sponsor: David Fisher, 311 Commonwealth Avenue, Boston.

SILVEUS, ESTHER, 591 Beacon Street, Boston.
University of Pittsburgh School of Medicine, 1932.

WALLACE, THOMAS E., 79 Payson Street, Revere.
Middlesex University School of Medicine, 1936. Sponsor: John T. Williams, 429 Beacon Street, Boston.

YURKANIS, EDWARD F., 1654 Columbia Road, South Boston.
Middlesex University School of Medicine, 1939. Sponsor: William R. Morrison, 520 Commonwealth Avenue, Boston.

Hollis L. Albright, *Secretary*
412 Beacon Street, Boston

WORCESTER DISTRICT

BOYD, JAMES G., Box 288, Westboro.
Boston University School of Medicine, 1939.

JOHNSON, WALFRED, 140 Central Street, Auburn.
Washington University School of Medicine, 1922.

MICHALSKI, KASIMIR S., 15 Vernon Street, Worcester.
Middlesex University School of Medicine, 1923. Sponsor: Benjamin F. Andrews, 36 Pleasant Street, Worcester.

MINSKY, JOSEPH W., 40 Central Street, West Boylston.
Mid West Medical College, 1934. Sponsor: Oscar Feinsilver, 390 Main Street, Worcester.

RICE, THEODORE A., 40 Whitman Road, Worcester.
Harvard Medical Schoool, 1938.

Leslie P. Leland, *Secretary*
36 Pleasant Street, Worcester

WORCESTER NORTH DISTRICT

LAMB, MARSHALL A., 20 Walnut Street, Winchendon.
Tufts College Medical School, 1939.

SCHECHTMAN, HAROLD I., 64 Milk Street, Fitchburg.
Middlesex University School of Medicine, 1934. Sponsor: Joseph D. Quinlan, 44 Prichard Street, Fitchburg.

Edward A. Adams, *Secretary*
44 Oliver Street, Fitchburg

DEATHS

BAILEY — WILLIAM T. BAILEY, M.D., of Boston, died January 16, in his seventy-fifth year.

Dr. Bailey received his degree from Harvard Medical School in 1900. He was a member of the Massachusetts Medical Society and the American Medical Association.

HARDING — EDWARD M. HARDING, M.D., of Newton, died December 19. He was in his ninety-first year.

Dr. Harding received his degree from the College of Physicians and Surgeons, New York, in 1874. At one time he served as second assistant physician at the Danvers State Hospital. He was a member of the Massachusetts Medical Society and the American Medical Association.

PHILBRICK — ROSCOE H. PHILBRICK, M.D., of New Orleans, Louisiana, died recently. He was in his sixty-third year.

Dr. Philbrick received his degree from Harvard Medical School in 1904. He was a member of the Massachusetts Medical Society and the American Medical Association.

TEMPLE — WILLIAM F. TEMPLE, M.D., of Boston, died December 25. He was in his fifty-sixth year.

Dr. Temple received his degree from the Harvard Medical School in 1911. He was past president of the Boston Society of Anesthetists. He served on the staff of the Massachusetts Women's Hospital. He was a member of the Massachusetts Medical Society and the American Medical Association.

MISCELLANY

NOTE

The commencement exercises of Middlesex University were held at New England Mutual Hall, Boston, on February 19. The degree of Doctor of Medicine was conferred on seventy-one successful candidates. Under the accelerated wartime program, instruction in the medical school will be resumed on March 17.

CORRESPONDENCE

FLORENCE CRITTENTON LEAGUE

To the Editor: May I call the attention of your readers to the facilities of our maternity home and hospital for the care of illegitimately pregnant girls and their babies.

The Florence Crittenton League maintains an ideal institution for the care of unmarried mothers — a unit home on the cottage plan with adequate hospital facilities surrounded with sufficient space for privacy to ourselves and to our neighbors. We also give expert care to girls who have the double misfortune of facing motherhood out of wedlock and of being afflicted with venereal disease. The physicians and social workers on the staff are experienced, and the Board of Directors is firmly convinced that the care rendered by the institution is unequaled. Hence, the Board is anxious to inform every community in New England, particularly in Massachusetts, that the maternity home and hospital exists and that we are prepared to help to the best of our ability the people of any community in matters connected with the problem of unmarried mothers.

The Florence Crittenton Home and Hospital, located at 10 Perthshire Road (Oak Square), Brighton, is the only institution of the Florence Crittenton Mission in New England. It offers prenatal, natal and postnatal care, and provides the following: cheery and comfortable rooms and dormitories for 23 expectant mothers; a hospital department including 21 beds with dental, operating-room and delivery-room suites; 33 cribs in sunny and well-ventilated nurseries and a completely equipped isolation unit consisting of 6 beds, a delivery room and a 6-crib nursery for the care of venereal-disease cases; expert medical, obstetric, pediatric and dental care in co-operation with the Boston Lying-in Hospital, Massachusetts General Hospital, Harvard Medical School and Forsyth Dental Infirmary; a large, sunny and airy 10-bed dormitory for convalescent mothers; a large, comfortably furnished living room for all classwork and recreation, with an adjacent well-equipped library; a fittingly furnished chancel adjoining the assembly room, which is opened for all devotional services; a social-service department with two trained workers, who help each girl and her family in making plans for her baby and her return to the community; and training under experienced workers in all household arts (cooking, nutrition, sewing and dressmaking), English, Red Cross home nursing, leather and metal tooling, and religious education. The charges are $7 per week for board and $30 for confinement, which are less than one third of the cost of the average case.

Applications should be made to the Superintendent, 10 Perthshire Road, Brighton, Massachusetts (STAdium 7600). If a girl is refused admission, other sources of care are advised and she is followed by the case worker until plans are completed.

Our girls live with us for an average of five months. The mental, moral and physical care necessary for rehabilitation is obtained through a normal family life, which many of them have never known. Wholesome recreation is a vital part of our program, and includes dramatics, current events, reading and discussions, as well as special events for all holidays. Much follow-up work is done by the two case workers in helping the girls in their readjustments to the community and to the care of their babies. Such service is given to every girl as long as she needs help, and many of these friendly relations continue for indefinite periods.

CLARENCE R. PRESTON, *General Secretary*

88 Tremont Street
Boston

(Notices on page xi)

NOTICES

TUFTS COLLEGE MEDICAL SCHOOL ALUMNI ASSOCIATION

The Hon. Paul V. McNutt, chairman of the War Manpower Commission, Washington, D. C., will be the guest speaker at the annual Tufts College Medical School Alumni Dinner on Wednesday evening, March 31, at the Copley-Plaza Hotel.

Other speakers on the program are Dr. Leonard Carmichael, president of Tufts College, who will talk on the medical school and the war, Dr. A. K. Paine, president of the Alumni Association, who will discuss alumni activities, and Dr. Fred W. Moroney, who will speak on the topic "The Twenty-Five-Year Class."

MASSACHUSETTS SAFETY CONFERENCE ON WAR PRODUCTION AND CIVILIAN DEFENSE

The annual Massachusetts Safety Conference on War Production and Civilian Defense will be held at the Hotel Statler, Boston, on March 29 and 30. Two of the sessions of particular interest to the medical profession are as follows:

WORKER HEALTH IN WARTIME (March 29, 10 a.m.). *Chairman*: Louis R. Daniels, M.D., medical director, Hood Rubber Company.

"Chlorinated Solvents in Common Wartime Use." Dohrman H. Byers, chemist, Massachusetts Division of Occupational Hygiene.

"Food for Production." Quindara Oliver Dodge, associate professor of institutional management, Simmons College.

"Safeguarding the Radium Dial Painter." Robley D. Evans, associate professor of physics, Massachusetts Institute of Technology.

MEDICAL SERVICE IN WARTIME INDUSTRY (March 30, 10 a.m.). *Chairman*: Thomas L. Shipman, M.D., works physician, General Electric Company.

"Coronary Heart Disease: Its threat to industry." Paul D. White, M.D., physician, Massachusetts General Hospital.

"The War Worker's Commonest Affliction — Dermatitis." George E. Morris, M.D., physician, Massachusetts Division of Occupational Hygiene.

"What Is IV-*F* in Industry?" Daniel L. Lynch, M.D., medical director, New England Telephone and Telegraph Company.

NEW ENGLAND PEDIATRIC SOCIETY

There will be a meeting of the New England Pediatric Society on Wednesday, March 24. The clinical presentation will be held at the White Amphitheater, Room 3A, Massachusetts General Hospital, and all other events at Longwood Towers, Brookline.

PROGRAM

4:00 Clinical Meeting: Examples of endocrine diseases in children. Dr. Allan M. Butler and his associates.
6:30 Refreshments.
7:00 Dinner.
8:00 Annual meeting of the society.
8:30 Panel Discussion: Current epidemic respiratory diseases in children. Dr. Chester S. Keefer, chair-

(Notices continued on page xiii)

WOUND INFECTION

its prevention and control

. . . in Lacerations

Treatment of lacerated wounds is assuming an increasingly important role in both military and civilian practice. It should be assumed that such wounds, since they are produced other than with surgical intent, are infected and must be treated accordingly. Generally recognized as the most important factor in delaying wound healing, infection must be controlled to reduce the period of partial or total disability.

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man, and Drs. John A. V. Davies, Maxwell Finland and Charles A. Janeway.

Questions are solicited on the subject for panel discussion and should be sent to Dr. James Marvin Baty before March 19.

NEW ENGLAND HEART ASSOCIATION

An extra meeting of the New England Heart Association will be held on Monday, March 22, at 8:15 p.m., at the Boston Medical Library.

Program

Continuous Recording Electrocardiography. Dr. William Likoff, Mr. M. B. Rappaport and Dr. Samuel A. Levine.

Respiration and Circulation in Patients with Pleural Effusion. Drs. M. D. Altschule and Norman Zamcheck.

Neurocirculatory Asthenia. Drs. Mandel Cohen, William Chapman, Stanley Cobb and Paul D. White.

Coronary Sinus Occlusion to Improve the Circulation to the Heart. Dr. Mercier Fauteux.

Underlying Causes of Arterial Embolism. Dr. Moises Levy and Robert R. Linton.

Interested physicians and medical students are cordially invited to attend.

AMERICAN COLLEGE OF CHEST SURGEONS

At a meeting of the Board of Regents of the American College of Chest Surgeons, held in Chicago on February 14, it was voted to cancel the 1943 annual session, which was scheduled to be held jointly with the annual meeting of the American Medical Association. The Board recommended that, wherever feasible, state and district chapters meet jointly with their state and district medical societies and assist in preparing scientific programs concerning chest surgery.

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Sunday, March 14

Monday, March 15

*12:15–1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital amphitheater.

Tuesday, March 16

*9:00–10:00 a.m. Medical clinic. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*12:00 m. The Mechanisms of Head Injury. Dr. Alan R. Moritz. South End Medical Club. Headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston.

*12:15–1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital amphitheater.

Wednesday, March 17

*9:00–10:00 a.m. The Clinical Significance of the Administration of Amino Acids for the Maintenance of Nitrogen Equilibrium. Dr. Paul Hecht. Joseph H. Pratt Diagnostic Hospital.

*12:00 m. Clinicopathological conference. Children's Hospital.

Thursday, March 18

*9:00–10:00 a.m. Medical clinic. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

(Notices continued on page xv)

63rd Year

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ELSIE S. NEUSTADT, M.D.

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FRIDAY, MARCH 19

*9:00–10:00 a.m. Gastrointestinal Hemorrhage. Dr. Fernando Biguria. Joseph H. Pratt Diagnostic Hospital.

SATURDAY, MARCH 20

*10:00–11:30 a.m. Medical staff rounds. Peter Bent Brigham Hospital.

*Open to the medical profession.

MARCH 22. New England Heart Association. Page xiii.

MARCH 24. New England Pediatric Society. Page xi.

MARCH 29 and 30. Massachusetts Safety Conference on War Production and Civilian Defense. Page xi.

MARCH 31. Tufts College Medical School Alumni Association. Page xi.

APRIL 5 and 6. Association for the Study of Internal Secretions. Page xi, issue of February 25.

MAY 19–25. American Board of Obstetrics and Gynecology. Page xii, issue of March 4.

MAY 25 and 26. Massachusetts Medical Society. Hotel Statler, Boston.

JUNE 4 and 5. American Board of Ophthalmology. Page xii, issue of March 4.

DISTRICT SOCIETIES

BRISTOL SOUTH

MAY 6. New Bedford.

ESSEX NORTH

MAY 5.

ESSEX SOUTH

APRIL 7. Addison Gilbert Hospital, Gloucester.

MAY 5. Salem Country Club.

FRANKLIN

MAY 11. Annual meeting.

Meetings are held at 11:00 a.m. at the Franklin County Hospital, Greenfield.

HAMPSHIRE

MAY 5.

MIDDLESEX EAST

MARCH 17. Bear Hill Golf Club, Stoneham, 12:15 p.m.

MAY 5. Bear Hill Golf Club, Stoneham, 6:30 p.m.

MIDDLESEX NORTH

APRIL 28.

JULY 28.

PLYMOUTH

MARCH 18. Goddard Hospital.

APRIL 15. Bridgewater State Farm.

MAY 20. Lakeville.

WORCESTER

APRIL 4. Hahnemann Hospital, Worcester.

MAY 12. Annual meeting.

WORCESTER NORTH

APRIL 28.

JULY 28.

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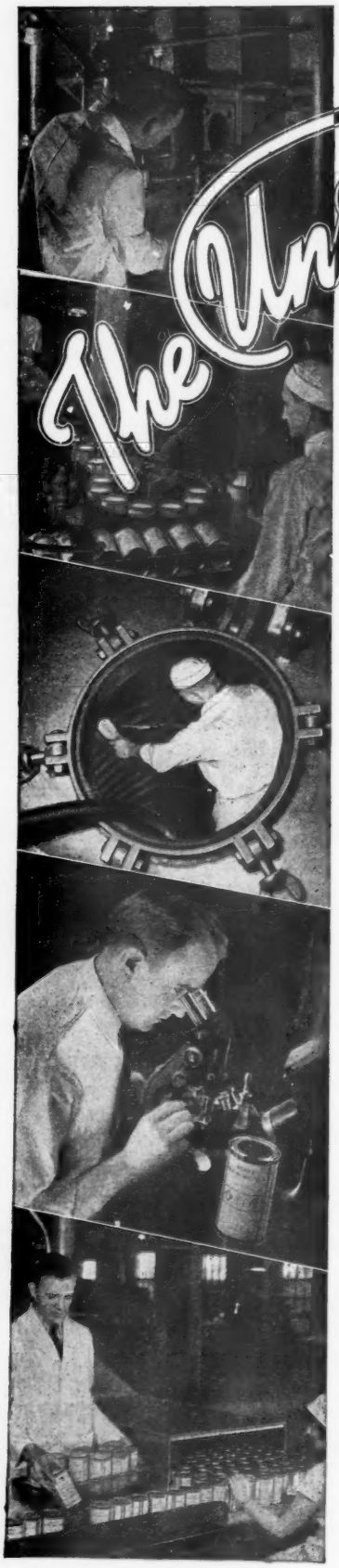

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